Marine Life Information Network
Marine Biological Association of the United Kingdom

MARLIN – MARINE LIFE INFORMATION NETWORK

SENSITIVITY ASSESSMENT OF CONTAMINANT PRESSURES

MYTILUS SPP. – EVIDENCE REVIEW

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To:

Joint Nature Conservation Committee, Defra, DAERA, Natural England, Natural Resources Wales, NatureScot, and Marine Scotland

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1 *Mytilus* spp. - Evidence review

The initial searches (01-15 June 2021) resulted in 9,197 hits of which 6,412 were duplicates. Therefore, only WoS and ECOTOX were used due to time constraints. The resultant 3,337 references were screened for relevance based on the proposed REA protocol. Stage 1 and stage 2 screening against the exclusion criteria reduced this number to 664 articles, which were taken forward for detailed review.

1.1 *Mytilus* spp. - Hydrocarbons and PAHs

The 143 articles relevant to the effects of 'Hydrocarbons and PAHs' and subject to detailed review are shown in 'Mytilus-evidence-summary-Mar2022.xls' (attached). Several review articles and additional papers were added to the list based on evidence cited within other papers. A further 25 articles were excluded at this stage after reading of the paper in detail.

- The majority of papers (ca 70%) were excluded at stage 2 screening because they examined bioaccumulation of contaminants, focused on the use of blue mussels (*Mytilus* spp.) to monitor or detect contaminants, or the use of numerous biomarkers to detect contaminants rather than the effect of contaminants on the mussels themselves.
- Another 25 papers were excluded at stage 3, after closer inspection of the papers, as they discussed monitoring studies, bioaccumulation, or biomarkers but, importantly, provided no information on the effect of hydrocarbon contaminant on *Mytilus* spp.
- Only 46 papers (7%) of those screened at stage 2 could not be accessed (at this stage).
- Most papers examined the effects of PAHs (27%); while the most commonly examined hydrocarbon contaminants were crude oils (22%), oil spills[1] (12.5%), fuel oils (12.5%), or multiple types of hydrocarbons (16%).
- While most papers used standard techniques to determine body burdens and detect a wide range of hydrocarbons, there was considerable variation in experimental design between studies. Therefore, it is difficult to compare results between studies.

Resistance assessment, as defined under MarESA, is based on the level of mortality reported in the evidence compiled in the literature review, as stated in the 'review question'. Evidence of lethal or sub-lethal effects was recorded in the evidence review. Where mortality was reported, the level of mortality was ranked using the resistance scale as 'severe', significant', 'some' or 'none.

Hydrocarbons were reported to cause a 'lethal' response in only 25% of the articles examined (Figure 1.1**.** Number of articles examined that reported lethal and sub-lethal effects to a range of hydrocarbon contaminants in *Mytilus* spp. (NR= not reported).). Most of the articles (70%) only reported and/or examined sub-lethal effects.

Where a lethal response was reported, only four articles (3.5%) reported 'Severe' mortality, but 12 (11%) reported 'Significant' mortality, and 12 (11%) reported 'Some' mortality (Figure 1.2). No mortality was reported in only 22% of the articles examined.

'Severe' mortality was only reported in four articles, two concerning exposures to crude oil, one to lubricant oil and one exposure to the water accommodated fraction (WAF) of fuel oil. Significant mortality was reported due to exposure to oil spills (two articles), crude oil (three articles), and fuel oil (six articles). Although PAHs were the most studied group of hydrocarbons, 'some' mortality was only reported in two articles, and the remaining 28 articles reported sub-lethal effects.

[1] Oil spills included instances of crude and fuel oils of different grades

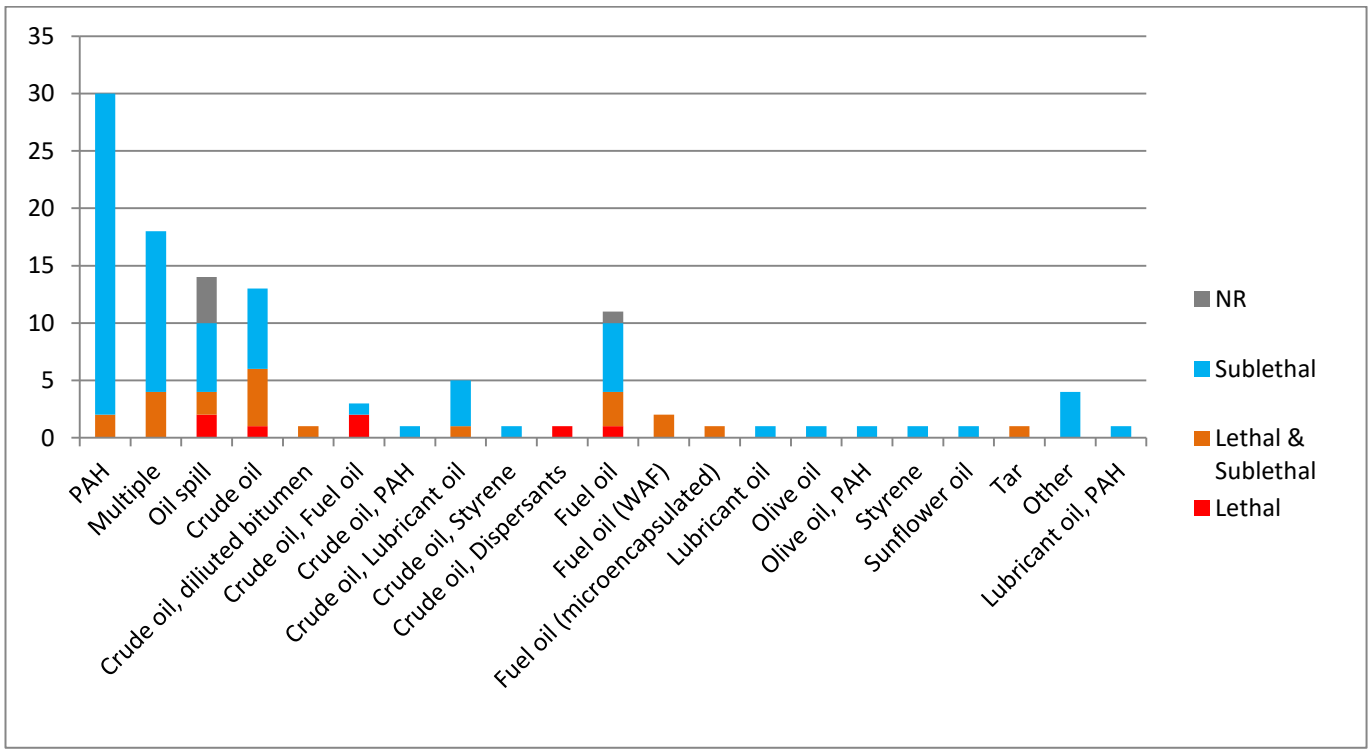

Figure 1.1. Number of articles examined that reported lethal and sub-lethal effects to a range of hydrocarbon contaminants in *Mytilus* spp. (NR= not reported).

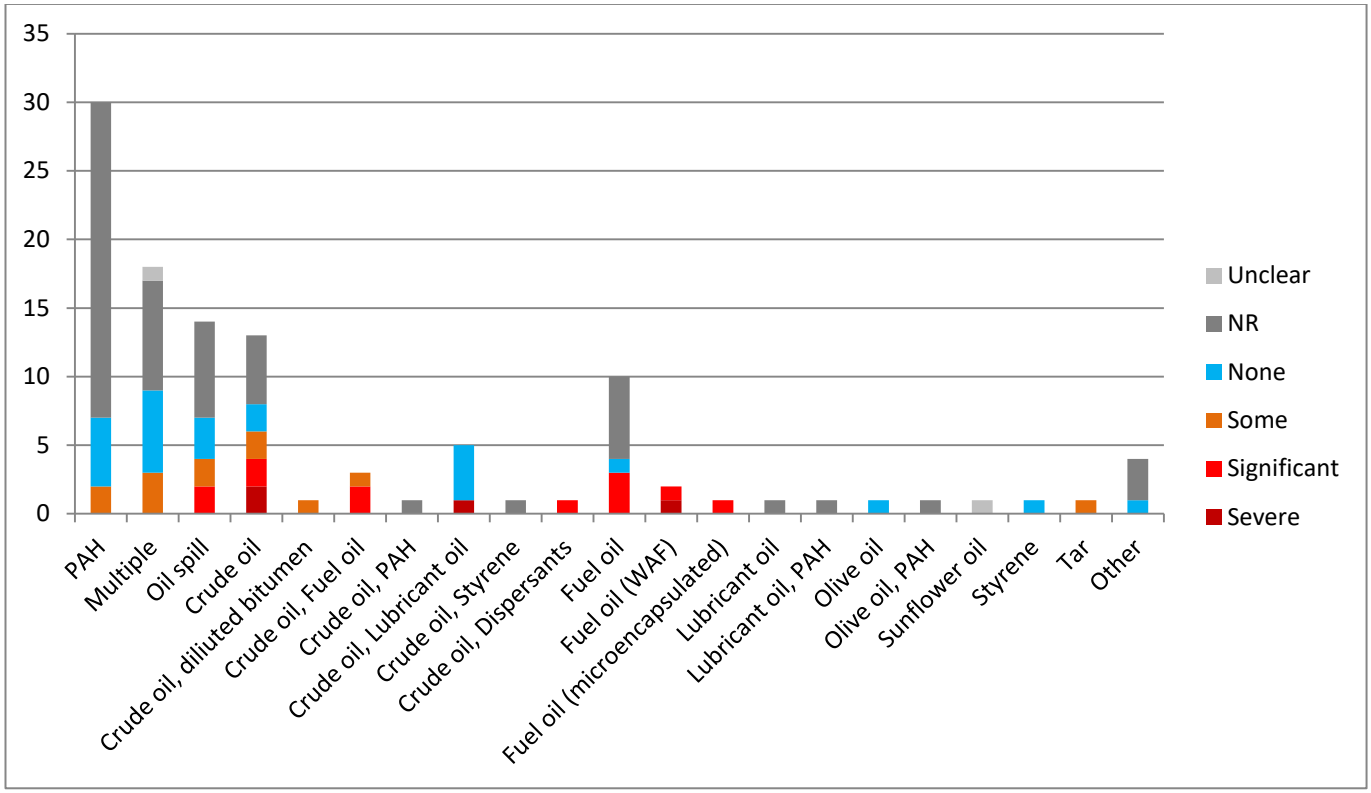

Figure 1.2. Count of ranked mortality (from 'severe' to 'none') in articles examined to a range of hydrocarbon contaminants in *Mytilus* spp. (NR= not reported).

Mortality was sometimes unclear or not mentioned in the studies examined. Mortality was 'not reported' in 50% of studies overall. However, most studies only examined sub-lethal effects.

A range of 'sub-lethal' effects were examined in the articles reviewed (Table 1.1). Most of the sub-lethal effects related to the use of mussels as biomarkers and few were informative about sensitivity.

Overall, the evidence collated demonstrates that hydrocarbons can cause direct mortality in adult and larval *Mytilus* spp. However, the variation in the experimental design makes it difficult to rank the relative mortality and/or resistance to hydrocarbons.

Table 1.1. Range of sub-lethal effects examined in the articles reviewed.

Sub-lethal effect	No. articles
Physiology	36
Accumulation	29
Mortality	29
Immunotoxicity	21
Histology	17
Genotoxicity	16
Toxicology	12
Proteomics	9
Reproduction	8
Feeding behaviour	8
Histochemical	7
Behaviour	7
Community	6
Other	15

The following evidence summaries and sensitivity assessments are based on the evidence collated in the literature review with an emphasis on evidence of mortality or sub-lethal effects that could result in population effects.

1.1.1 Oil spills.

***Torrey Canyon* 1967 (crude oil).** Smith (ed., 1968) reviewed information on the effects of the *Torrey Canyon* oil spill in 1967. *Mytilus edulis* was reported as missing from Porthleven, although Smith (1968) noted that it was more characteristic of the exposed north coast where they were found to be quite resistant of oil alone and moderate doses of detergent but “not intense” treatment. Mussels survived in Booby's Bay which was subject to heavy oil but no detergent treatment. Oil was noted amongst small mussel shells on rocks from which it had been washed off. Mussels were found behaving normally and alive in rock pools which had a film of oil at Portreath even though their mantle cavity contained globules of oil.

***Sea Empress* 1996 (crude oil)**. Crump *et al.* (1999) examined a set of permanent quadrats in Manorbier and West Angle Bay, Pembrokeshire, before and after the *Sea Empress* oil spill. At Manorbier, large numbers of small mussels were reported amongst crevices and cracks in the middle shore. Crump *et al.* (1999) noted that 'chocolate mousse' coated large areas of the rocky platform but tended to collect in gullies and crevices. Manorbier is a steep rocky, wave exposed, shore so most of the quadrats were clear of oil by the 28th February, 13 days after the spill. Coralline algae showed significant bleaching but there was no clear evidence of mortality or ill effects on the other organisms surveyed in their quadrats.

Moore (1997) examined rocky shore transects set up in Milford Haven shortly after the Sea Empress oil spill. Moore (1997) noted a slight increase in *Mytilus* abundance across sites between 1995 (pre-spill) and 1996 (after spill) but suggested that it was natural variation unlinked to the oil spill. Morrell (1998) examined permanent transects at Dale Fort set up after the Sea Empress oil spill. There was little

obvious effect on *Mytilus edulis* in Castel Beach Bay and Monkhaven where numbers were stable, except for one site at Monkhaven where the mussels were lost ca 11 months after the spill. However, the cause was uncertain.

Roston & Bunker (1997) survey sublittoral epibenthic rock communities, 16 months after the *Sea Empress* oil spill. One site included a subtidal *Mytilus edulis* bed habitat at 8-10 m. Samples were taken for hydrocarbon contamination measurement and revealed 12-17 ppm (although dwt or wwt not mentioned). Overall, all the habitats examined (inc. *Mytilus edulis*) were in normal condition and showed no effects of the oil spill.

***Exxon Valdez* 1989 (crude oil).** Highsmith *et al.* (1996) surveyed intertidal communities affected by the *Exxon Valdez* oil spill between spring 1990 and summer 1991, ca 1-2 years after the spill (Dec. 1989). *Mytilus trossulus* abundance and biomass were significantly reduced at most oiled sites studied compared to reference sites. Where the biomass was higher on oiled sites this was attributed to the survival of large individuals over smaller individuals. Highsmith *et al.* (1996) suggested that recovery had started at some Prince William Sound's sheltered rocky and estuarine shore, with no significant difference between oiled and reference sites by summer 1991. However, at coarse sediment and estuarine sites in Cook Inlet and Kenai Peninsula the differences were still significant, indicating that recovery was still in progress.

Conversely, Thomas *et al.* (1999) found no significant trends in byssal thread production or condition index between mussels from polluted sites and mussels from clean sites. However, mussels collected from oiled sites had significant PAH concentrations in their tissues compared to mussels from the reference sites.

Babcock *et al.* (1998) reviewed the effects of oiling from the *Exxon Valdez* on blue mussel beds (*Mytilus trossulus*) in Prince William Sound. Many of the oiled mussel beds in the Sound were not subject to cleaning due to their commercial value. Babcock *et al.* (1998) reported that the presence of the mussel bed retained the oil contaminant within the underlying sediment, preventing its breakdown or removal by wave action. As a result, the mussels remained contaminated and a threat (via consumption) to wildlife. Mussel condition was adversely affected by oil but some physiological measures in mussels contaminated for 3-4 years were not correlated with oil concentration. No mortality of mussels on the beds was reported, either directly related to oiling after the spill or to PAH contamination.

***Erika*, 1999 (heavy fuel oil).** Amat *et al.* (2004) demonstrates a genotoxic event on the digestive glands of the mussels living in the coast impacted by the Erika spill. Immediately after the Erika accident (December 1999 and January 2000), a very high amount of DNA adduct could be observed even in the reference site. Unfortunately, no data on the occurrence of adducts before the spill was available.

***Prestige* 2002 (heavy fuel oil)**. Peteiro *et al.* (2006) investigated whether the *Prestige* oil spill effected the growth of *Mytilus galloprovincialis* seed collected from three different populations along the coast of northwest Spain three months after the spill (February 2003). The results showed the mussels from the area most affected by the spill to have significantly less growth in terms of weight. In addition, the percentage of mussels classified as 'large' from the population most affected by the spill was significantly less than the other two populations. No significant difference in growth or biochemistry was noted in the mussel seed collected in 2004, which suggested the absence of sub-lethal effects in the offspring of mussels exposed to the spill (Peteiro *et al.,* 2006). However, Labarta *et al.* (2005) found mussel seed from sites with the greatest oil impact had the lowest survival performance in air, with the lowest survival rates observed from a site that exhibited the highest PAH values.

***Hebei Spirit* 2007 (crude oil).** Jung *et al.* (2015) examined the effects of the *Hebei Spirit* oil spill on intertidal habitats in Korea, nine months after the spill. *Hebei spirit* spilt ca 10,900 t crude oil in poor weather with strong wave action. After nine months, the density of all Mollusca, including *Mytilus galloprovincialis* was significantly reduced at impacted sites compared to controls. Donaghy *et al.*

(2016) found mussels from two polluted sites following the *Hebei Spirit* oil spill to have a significantly lower condition indices than the control site.

***Kimya* 1991 (sunflower oil).** Mudge *et al.* (1993) examined the levels of fatty acids in *Mytilus edulis* around Anglesey after the *M.V. Kimya* spill of sunflower oil in January 1991 at Bodorgan Head. Components of the sunflower oil were incorporated into flesh of mussels around Anglesey but enhanced levels of linoleic acid (18:2 w6) (the best indicator of sunflower oil contamination) was limited to a 3 km wide area centred on the wreck. They concluded that mussels were able to metabolise fatty acids from the spill. A large mortality of mussels occurred at Aberffraw in June 1991, but it could not be attributed to the sunflower oil conclusively.

Others. The *Esso Bernica* spill (Sullom Voe, 1978) had little effect of intertidal communities in un-cleared areas (Rolan & Gallagher, 1991). The *Braer* spill (Shetland 1993) removed grazers (although it may have also been due to the use of dispersants), and no change in *Mytilus* abundance was reported (Newey & Seed, 1995).

Sensitivity assessment (oil spills)

Little evidence on the direct physical effects of oil (smothering, or clogging) on *Mytilus* spp., was found and few studies examined blue mussel beds, except in Babcock *et al.* (1998) and Rostron & Bunker (1997). The evidence suggests that *Mytilus* spp. can be relatively tolerant of direct oiling (in the absence of dispersants or other cleaning treatments) and survived oil spilt by the *Torrey Canyon* and *Sea Empress*. In particular, blue mussel beds in Prince William Sound (Babcock *et al.*, 1998) survived direct oiling and continued exposure to oil retained in the sediment underneath the mussel beds for 3-4 years, although their condition was impaired. However, *Mytilus trossulus* abundance in other intertidal habitats was significantly reduced after the *Exxon Valdez* spill (Highsmith *et al.,* 1996). In addition, a significant reduction in *Mytilus galloprovincialis* abundance was also noted after the *Hebei Spirit* spill in Korea (Jung *et al.,* 2015). Hence, the effect of oil spills on *Mytilus* spp. and blue mussel beds is likely to be dependent on the type of oil spilt, the local habitat, and wave conditions at the time of spill. Therefore, resistance is assessed as '**Low'** to represent the potential for mortality. Resilience is probably '**Medium**' so sensitivity to oil spills is assessed as '**Medium**'.

1.1.2 Petroleum hydrocarbons (oils)

Lethal effects of exposure to hydrocarbons were only reported in 25% of the articles examined. Only 11 of the papers examined provided details of LC_{50}, LT_{50}, or EC_{50} values based on laboratory studies. The lethal effects of petroleum oils (e.g. crude oil, fuel oils, and lubricant oils) are summarized below and reported LC_{50} or LT_{50} values for petroleum hydrocarbons (i.e. oils) are shown in Table 1.2. Information on the effect of oil contamination on 'scope for growth' (SFG) (Widdows & Johnson, 1988; Widdows & Donkin, 1992) or other condition indices is also included.

- Saco-Alvarez *et al.* (2008) exposed developing *Mytilus galloprovincialis* larvae to WAF of Prestige oil and Marine fuel oil under light and dark conditions. The EC_{50} (50% larval abnormalities 48 hours) was 13% WAF irrespective of light regime, while the EC_{50} was 20% Marine WAF in the light treatment and >100% in darkness EC_{50}. Undiluted Marine WAF only caused a 20% decrease in mussel normal larvae.
- Swedmark *et al.* (1973) examined the exposure of *Mytilus edulis* to several dispersants, dispersant and fuel oil mixtures and Oman crude oil. The LC_{50} after 96 hr exposure to Oman crude oil and 48 hr recovery in clean seawater was >1000 ppm.

Table 1.2. Examples of LC_{50}, LT_{50}, or EC_{50} values for the effects of oils on *Mytilu*s spp..

Contaminant	Exposure Conc.	Exposure duration	Life stage	LC/EC_{50}	Short Reference
Oman Crude oil	350, 650, 1000 ppm	96 hours	Adults	LC_{50} 96 hr =<1000 ppm	Craddock, 1977; Swedmark *et al.*, 1973
Crude oil	NR	48 hours (embryogenesis), 5 days (mortality)	Larvae, Embryos (blastula / trochophore) (20 hours)	EC_{50} 48h embryogenesis = 2000 µg/l, LC_{50} 5days = 2-4 ppt	His *et al.*, 2000
Crude oil weathered and non-weathered Fresh oil: Mass, Q4000 Weathered oil: CTC, Juniper Corexit 9500A	NR	48 hours	Larvae	LC_{50} Fresh oil: Mass >100% WAF LC_{50} Fresh oil: Q4000 >100% WAF LC_{50}Corexit 9500A 25-45% WAF LC_{50} Mass + Corexit 9500A 20-35% WAF LC_{50} Q4000 + Corexit 9500A 20-30% WAF	Stefansson *et al.*, 2016
Tar	60, 80, 100, 120, 140, and 160 mg/l (acute toxicity test) 10, 40, 60 mg/l (condition test)	96 hours (acute toxicity test) 17 days (condition test)	Adults	LC_{50} =139.84 mg/l Tar	Alonso *et al.,* 2019
Diesel oil (microencapsulated), copper	5,10,30,50,100, 500 µg/l (larvae) 200, 600, 1000, 1300, 5000 µg/l (adults)	10 days larvae, 30 days adults	Adults, Larvae	EC_{50} (30 days) = 800 µg/l; LC_{50} (30 days) adults ca 5000 µg/l diesel oil (microencapsulated)	Strømgren & Nielsen, 1991; His *et al.*, 2000

- Schmutz *et al.* (2021) examined the effects of oil spill exposure under ice on caged mussels (*Mytilus edulis*), during the spawning season, and their resultant larvae in experimental mesocosms, using crude oil and diluted bitumens. Mussels were exposed to Heidrun and North Sea crude oil, and Cold Lake Blend and Access Western Blend diluted bitumen from Canadian oil sands. Bioaccumulation of PAHs was detected three days after exposure. Higher concentrations were associated with the crude oil (5.49 +/- 0.12 µg/g dwt) than both diluted bitumens (0.51 +/- 0.03 or 0.91 +/- µg/g dwt). Clearance rates were significantly reduced by Heidrun crude oil and Cold Lake Blend diluted bitumen. Cellular stress (lysosomal stability) was highest under each oil treatment, and byssus thickness was significantly lower under each oil treatment. However, there was good recovery and the negative effects on some biomarkers disappeared one month afterwards. Mortality was not excessive and never more than 15% in each treatment (Schmutz *et al.*, 2021). Gametogenesis and larval development were affected for a longer period. Gonad development was lower in oil treatments but showed no recovery after a month. Spawning was induced several weeks after treatment. Embryogenesis and larval development were severely affected, with larval development lagging five days behind the controls.
- Cajaraville *et al.* (1992) examined the effect of WAF of two types of crude oil and one type of commercial lubricant oil on the physiology of *Mytilus galloprovincialis*. A few mussels died in the

crude oil treatments, irrespective of dose. However, exposure to the refined lubricant oil resulted in 100% mortality after 49 days at the high dose (40% WAF in seawater) and 77 days at the intermediate dose (6% WAF). They noted that Ural oil WAF was more toxic than Maya oil WAF due to higher concentrations of aromatic hydrocarbons in Ural oil WAF, although the lubricant oil had the highest concentration of aromatic hydrocarbons. Overall, exposure to the crude and refined oil WAFs significantly reduced growth of shell and flesh, and affected health, reproduction and survival.

- Alonso *et al.* (2019) estimated the LC_{50} (96-hour) of tar at 139.84 mg/l in *Mytilus galloprovincialis*. Alonso *et al.* (2019) also observed gonadal condition index of mussels exposed to 60 mg/l tar to be significantly reduced after 10 days, and after 17 days, the gonadal condition index of mussels in the 10 and 40 mg/l treatments was also reduced. Histological findings showed spermatogenesis disruption and alterations of somatic and germinal cells as a direct effect of treatment.
- Børseth *et al.* (1995) found oil, oil dispersants, formaldehyde, and benzene to cause the sodium gradient across cell membranes to drop and caused the death of some test organisms. Phenol had an anaesthetic effect (at 100 mg/l) but the depression in sodium gradient was not significant, and mussels recovered. Benzene and formaldehyde significantly decreased the sodium gradient. The oil and dispersant mixtures also significantly reduced sodium gradient. However, Boreth *et al.* (1995) stated that prior experiments found that exposure to benzene and formaldehyde at the stated levels for 5 days resulted in mortality and remarked that exposure to oil and dispersants at slightly higher concentrations or longer durations caused mortality but gave no supporting data.
- Ikävalko *et al.* (2006) investigated the use of cotton grass as oil sorbent in marine environmental protection. The addition of diesel to static tank experiments resulted in 100% mortality of *Mytilus* spp. and *Dreissena* spp. when exposed to diesel without the addition of cotton. However, the final concentration of diesel was not given.
- Lowe & Pipe (1987) examined the effect of diesel oil WAF (27.4 +/- 7.2 (Low) ppb and 127.7 +/- 28.3 (High) ppb total diesel oil hydrocarbons) on reproduction and survival in *Mytilus edulis* collected in summer when food reserves were high and in autumn when they were low. All treatments, including controls experienced mortality due to starfish predation and spawning stress between Jan-June. But in the following 80 days (June-Sept), mortality was highest in the High oil treatment (71% in mussels collected with low food reserves, and 27% in mussels with high food reserves), less in the Low oil treatment (14.5% and 12.6% as above) and zero in controls, which suggested that condition and season were factors in mortality from oil exposure.
- Stefansson *et al.* (2016) examined the toxicological effects of non-weathered and weathered crude oil from the *Deepwater Horizon* incident on the development of marine bivalve (*Mytilus galloprovincialis, Crassostrea gigas, Mercenaria mercenaria*) and echinoderm larvae. Weathered oils had no toxic effect on developing larvae. However, fresh oil had adverse effects on developing larvae. There was no significant difference in EC_{10} values between echinoderm and bivalve larvae. The average EC_{10} (abnormal development) values for the larval species exposed to these WAFs were 67±22 mg/l total PAH (46±18% WAF) and 66±19 mg/l total PAH (57±22% WAF) for fresh oil samples. Stefansson *et al.* (2016) gave LC_{50} values for *Mytilus* larvae of ca 130[2] µg/l TPAH and ca 140 µg/l TPAH for fresh oils but state that these values were higher than the highest concentration tested.
- Strømgren & Nielsen (1991) found microencapsulated diesel oil to reduce spawning frequencies of *Mytilus edulis* by 40-45% of the control at 1,000 and 1,300 µg/l. At 5,000 µg/l exposure, the spawning frequencies were negligible. The mortality of *Mytilu*s adults was around 40% when exposed to 5,000 µg/l microencapsulated diesel oil, with the LC_{50} (30-day) corresponding to about 5,000 µg/l. However, larval mortality rose steeply until 20-30% mortality at 50 µg/l and was 100% at 500 µg/l. The LC_{50} value (10-day) for larvae was found to be 30-35 µg/l. Larval growth was

[2] Approximate value extracted from graph/figure in text

significantly reduced at 10 µg/l, with an EC_{50} (10-day) of 24-30 µg/l; an order of magnitude less than the EC_{50} for growth of juvenile mussels (ca 1000 µg/l; Strømgren & Reisen, 1988 unseen). Therefore, they suggested diesel oil was, more toxic to larvae than juveniles. However, variation in larval mortality was higher between batches than variation in growth.

- Bokn *et al.* (1993) examined the effect of diesel oil WAF on littoral rocky shore communities in flowing water mesocosms, each including five steps to simulate tidal levels. The communities were allowed to establish in the mesocosms for 32 months prior to the experiment. Mesocosms were exposed to controls, High WAF (129.4 µg /l (mean)), and Low WAF (30.1 µg/l mean) for 24 months, and the communities were examined at three monthly intervals. *Mytilus* communities were the worst affected across the mesocosm. Their cover decreased to zero at all tidal levels within the High WAF mesocosm and the upper two tidal levels by the end of the study in the Low WAF mesocosm. At the lower tidal levels in the Low WAF mesocosm, the population of *Mytilus* was reduced to one individual by the end of the study. The population of *Mytilus* increased slightly in the control mesocosms. Bokn *et al.* (1993) noted that the decline in *Mytilus* cover corresponded to a decrease in byssal attachments and increased susceptibility to starfish predation.
- Baussant *et al.* (2011) exposed *Mytilus edulis* to dispersed crude oil (0.015-0.25 mg/l) for seven months across its entire gametic cycle to simulate the effect of produced water discharges from North Sea oil installations. Reduced fertilization success was observed when both adult mussels and gametes were exposed to 0.25 mg/l oil and only 60% of the eggs were fertilized. Larval development was affected by parental exposure to oil, causing abnormal growth. Adult and larvae exposure to oil resulted in a significantly smaller larva. Also, if only the adults or only the larvae were exposed to the oil, the larvae grew bigger than those in the adult larvae exposure, but the larvae were still significantly smaller than the control. There was a concentration-dependent increase in the volume density of atretic[3] oocytes in female mussels exposed to oil; females exposed to 0.25 mg oil/l had significantly higher volume density of atretic oocytes than control females. However, after spawning, the volume density of atretic oocytes was low and no differences between experimental groups were observed. When both adult mussels and their embryos were exposed to 0.25 mg oil/l, a significantly higher level of DNA strand breaks in the embryos one day post-fertilization was found. Overall, the study indicated a decrease in potential reproductive success and recruitment by mussels exposed to dispersed crude oil for months at 0.25 mg/l but Baussant *et al.* (2011) noted that 0.25 mg/l dispersed oil was probably restricted to with the first 0.5 km of a discharge point of North Sea oil platforms.
- Counihan (2018) used ecologically relevant concentrations of oil (10 ppm crude oil) and dispersant based on concentrations measured in dispersed oil field trials and after oil spills. Counihan (2018) observed 5% *Mytilus trossulus* mortality in treatments with non-dispersed crude oil and treatments with crude oil and Corexit 9500 (3.75%), however mortality in the treatments were low. After seven days, mussels in all the treatments had significantly thinner shells than the controls and after 21 days mussels in all treatments exhibited evidence of genetic damage, tissue loss and a continued stress response.
- His *et al.* (2000) reviewed the use of bivalve larvae as a monitor or biomarker for contaminants. In one example, His *et al.* (2000) reported a 48-hour EC_{50} embryogenesis of 2,000 µg /l, and 5-day LC_{50} of 2-4 ppt in *Mytilus edulis* larvae exposed to crude oil (Luca & Le Roux, 1975, cited in His *et al.*, 2000).
- Gomiero *et al.* (2015) found *Mytilus galloprovincialis* sampled from three gas field sites in the Adriatic in the summer months had a significant decrease in survival in air compared to the reference organisms. However, no significant difference was observed in winter collections.

[3] Degenerated and reabsorbed oocytes

- Widdows *et al.* (1982) used three experimental approaches to examine the effect of WAF crude oil on mussels. Experiment 1 examined the effect of hydrocarbons in food, while Experiment 2 examined hydrocarbon absorption and Experiment 3 examined long-term exposure. They reported that 30 µg/l WAF decreased feeding rate significantly and that 30-36 µg/l elevated respiration rate by 30%. Oxygen consumption increased after seven days and remained elevated for five months in the long-term experiment. In Experiment 1, mussels had negative SFG after 28 days. Overall, there was a correlation between the decline in SFG and increase in tissue aromatic concentrations, with negative SFG at ca >7 µg/g wwt of mussel tissue. Widdows *et al.* (1982) also noted that the 30-36 µg/l WAF concentrations used were comparable to levels found in the environment (e.g. the Thames in 1980) but that very high concentrations (5-1,000 mg/l) were required to elicit a lethal response in *Mytilus edulis* (see Craddock, 1977).
- Widdows *et al.* (1987) exposed *Mytilus edulis* to WAF diesel oil (125 +/- 28 µg/l High oil and 28 +/- 7 µg/l Low oil in tidal, flowing seawater mesocosms for eight months. Both low and high oil conditions resulted in a significant decrease in SFG mainly due to a reduction in feeding and food absorption. SFG was severely reduced in high oil conditions, resulting in weight loss as the mussels used tissue reserves. Widdows *et al.* (1987) reported a direct relationship between declining SFG and log of hydrocarbon concentration. SFG became negative at ca >30 µg/l WAF. However, no mortalities were reported in the eight-month exposure period, and all mussels had recovered 55 days after return to untreated seawater. They noted that mussels from the high oil treatment depurinated hydrocarbons and recovered faster than those exposed to the low oil treatment.
- Craddock (1977) reviewed the evidence of acute toxicity of marine organisms to petroleum. Craddock (1977) reported:
    - 0-100% mortality in *Mytilus californianus* collected from four locations, exposed to 10,000 ppm of the soluble and emulsified fractions of Santa Barbara crude oil for 48-56 hours; the larger mussels were the most susceptible;
    - 28.4% or 24.4% mortality in *Mytilus galloprovincialis* larvae exposed to 1,000 ppm of Venezuelan Crude oil or No. 1 fuel oil respectively;
    - 66% mortality in *Mytilus edulis* exposed to 10% Outboard motor effluent for 24 hours (and nine days holding);
    - a LC_{50} (96-hour) < 1,000 ppm in *Mytilus edulis* exposed to Oman crude oil. Note - <350 ppm lowest conc. affecting byssal activity and shell closure, <1,000 ppm lowest conc. affecting shell closure; Crude oil less toxic than emulsions;
    - an EC_{50} (loss of attachment and formation of byssus) in *Mytilus edulis* of 17 ppm WSF No. diesel oil after 24 hours and 15.6 ppm after 48 hrs; and
    - an EC_{50} (failure to reattach to substratum) in *Mytilus edulis* of 16.6 ppm after 24 hours and 15 ppm after 48 hours exposure to No. 2 diesel oil (layered on the surface and stirred constantly).

Sensitivity assessment (oils). Refined oils (e.g. lubricant and fuel oils) were reported to be more toxic than crude oils. Widdows *et al.* (1982) also noted that the 30-36 µg/l WAF concentrations used in their experiments were comparable to levels found in the environment (e.g. the Thames in 1980) but that very high concentrations (5-1,000 mg/l) were required to elicit a lethal response in *Mytilus edulis* (see Craddock, 1977). Overall, the evidence suggests (10% of articles on the effects of oils) that exposure to oils or their water saturated (WSF) or water accommodated fraction (WAF) can result in 'severe' mortality (>75%) while another 30% of the articles report significant (25-75%) mortality depending on the type of oil and its concentration. Therefore, resistance is assessed as **'None'**. Resilience is probably 'Low' so that sensitivity to petroleum-based oils is assessed as **'High'**.

In their review, Widdows & Donkin (1992) note that one reason mussels are good sentinels for pollution is because they are relatively tolerant of, but not insensitive, to a range of environmental conditions and contaminants. Furthermore, they noted that adults were >10-fold more sensitive than larvae to copper (Cu), petroleum hydrocarbons and sewage sludge. Widdows & Donkin (1992) suggested that LC_{50} values in *Mytilus* gave a false impression of high tolerance because adult bivalves were able to close their valves and isolate themselves from extreme (potentially lethal) conditions for long periods (i.e. days).

1.1.3 Polyaromatic hydrocarbons (PAHs)

Only three papers that examined the effects of PAH exposure reported 'some' mortalities, although not direct mortality but rather as LT_{50}s based on their 'survival in air'. Donkin *et al.* (1989) reported the EC_{50} (on feeding rates) for a range of PAHs. The remaining 27 papers concentrated on a range of sub-lethal effects as biomarkers of contamination (see below).

- Giannapas *et al.* (2012) exposed *Mytilus* spp. to phenathrene (0.1 mg/l), anthracene (0.1 mg/l) or a mixture (0.2 mg/l) for 7 days. They found that mussels exposed to PAHs to have reduced ability to survive in air with LT_{50} values in the range of 3-4 days, while control treatment mussels had an LT_{50} values of 7 days. The mussels from the PAH treatments also had lower cell viability, increased lysosomal acid phosphatise activity, high frequencies of micronuclei, and other abnormalities in haemocytes.
- Blanco-Rayon *et al.* (2020) examined the PAH and metal burden and suite of biomarkers in *Mytilus galloprovincialis* collected from two sites, Arriluze (highly polluted) and Plentzia (relatively clean) in the Bay of Biscay. They used LT_{50} in air examine the stress of the mussels. Although a highly polluted site, the mussels from Arriluze had a higher survival in air than those form Plentzia in all seasons. They suggested that a better nutritional state (of the Arriluze mussels) masked the negative effects of the pollutants.
- Eertman *et al.* (1993) examined 'survival in air' (LT_{50}) of *Mytilus edulis* transplanted to various sites in Dutch coastal waters for seven days. They concluded that increased tissue levels of PAHs and PCBs were correlated with decreased ability to 'survive in air'.
- Donkin *et al.* (1989) examined the effects of hydrophobic organic chemicals on the feeding rates of *Mytilus edulis*. Toxicity was confirmed by the concentration in mussel tissue required to reduce feeding rate by 50% (TEC_{50}). The concentration of contaminant in the water required to reduce clearance rates by 50% was also recorded. All of the contaminants in the study were found to reduce feeding rates.
- Widdows *et al.* (1995) examined scope for growth and body burden of contaminants (inc. hydrocarbons) in *Mytilus edulis* collected from North Sea coasts of the UK from Shetland to Whitstable. They reported a general increase in stress (reduced SFG) from the cleaner waters to north Scotland to the south of England. In the majority of the 26 coastal sites and 9 offshore sites, 90% of the decline in SFG was explained by PAHs. Polar organics, probably of natural origin, contributed to the decline at some sites.
- Widdows *et al.* (2002) examined SFG and various contaminant levels in mussels from 38 sites around the Irish Sea. A decline in SFG was associated with increased levels of contaminants. They reported that 50-80% of the decline in SFG was due to PAHs from fossil fuels and oil spills. TBT made a minor contribution to the decline in SFG while the metal concentrations at their sites tested were not high enough to have a significant effect.
- Granby & Spliid (1995) examined the concentrations of a range of hydrocarbons in *Mytilus edulis* around the Danish coast. They found a significant negative correlation between the condition index the total PAH concentrations and paraffin-naphthene (p-n-)-hydrocarbon concentrations in their tissues.

Sensitivity assessment (PAHs). Only a few articles demonstrated 'some' mortality (<25%) due to exposure to PAHs, and then indirectly, as a result of stress and subsequent reduction in the specimen's ability to survive in air. Similarly, Widdows and others (1995, 2002) demonstrated a decrease in condition or SFG due to PAH exposure and body burden. However, most articles examined (93%) only reported sub-lethal effects (Figure 1). Therefore, resistance is assessed as **'Medium'** to represent the 'worst-case' potential of PAHs to cause indirect mortality due to reduced condition and/or stress. Resilience is probably '**Medium**' so sensitivity to PAHs is assessed as '**Medium**'.

1.1.4 Others

- Sabourin & Tullis (1981) found Benzo [*a*] pyrene (B[*a*]P) (10 ppm), benzene (50 ppm) and toluene (100 ppm) to significantly reduce the heart rates of *Mytilus californianus*. Additionally, significant declines in the rate of oxygen consumption occurred for 50 ppm benzene, 10 and 100 ppm toluene and 1 ppm B[*a*]P. **Mortality was only observed in the 100 ppm toluene treatment** but mortality was not quantified.
- Smith *et al.* (2001) observed the feeding rates of *Mytilus edulis* to reduce significantly when exposed to 6-cyclohexyltetralin or 7-cyclohexyl-1-propyltetralin, with a linear relationship between exposure concentration and body burden observed.
- Mamaca *et al.* (2005) exposed adult *Mytilus edulis* to 0.2 mg/l of styrene for 7 days in a flow through laboratory experiment. No mortality was observed in the test specimens, but lysosomal membrane activity was significantly reduced, and DNA damage was significantly increased compared with controls.
- Danellakis *et al.* (2011) found olive oil mill wastewater (OMW) at the concentration of 1, 0.2, 0.1, and 0.01% v/v to have no effects on the survival of *Mytilus galloprovincialis* over a period of four days. However, high frequencies of either micronuclei or other abnormalities tested were found in haemocytes of mussels exposed to 0.01 or 0.1% (v/v) OMW. A concentration dependent increase in levels of DNA damage were detected in haemocytes. In addition, a significant inhibition of Acetylcholineesterase (AChE) activity was observed in the haemolymph and in the gills of mussels in the treatment groups. The treatment groups also showed significant increases in metallothionein activity and lipid peroxidation.

The evidence on 'other' forms of hydrocarbons was limited. Evidently, toluene is potentially toxic to *Mytilus* spp., while benzene, olive oil mill wastewater, styrene and 'tetralins' were reported to have sub-lethal effects at the concentrations studied.

1.1.5 Sub-lethal effects

Overall ca 70% of the articles examined only reported sub-lethal effects of the effects of hydrocarbons in *Mytilus* spp. This was because many studies examined the effects of contaminants on immunotoxicity, genotoxicity, proteomics, and other biomarkers, or examined exposure to field relevant concentrations of contaminants. Many of the biomarkers examined indicated 'stress' in the exposed mussels. However, it was difficult to understand if the resultant 'stress' would result in changes in the population. Further research is required on how relevant 'sub-lethal' effects are to sensitivity assessment, except where mortality, loss of condition, SFG, or changes in reproduction are shown (above) to affect the population adversely. Therefore, sub-lethal effects are not discussed further.

1.1.6 Sensitivity assessment - Hydrocarbons and PAHs.

In their review, Widdows & Donkin (1992) note that (one reason) mussels are good sentinels for pollution is because they are relatively tolerant of, but not insensitive, to a range of environmental conditions and contaminants. Furthermore, they noted that adults were >10-fold more sensitive than

larvae to copper (Cu), petroleum hydrocarbons and sewage sludge. Widdows & Donkin (1992) noted that lethal responses give a false impression of high tolerance since the adults can close their valves and isolate themselves from the environment for days. They suggested that sub-lethal effects e.g., shell growth and 'scope for growth' (SFG), were more sensitive indicators of the effects of contaminants.

The evidence review suggests that exposure to hydrocarbon contamination can cause mortality in *Mytilus* spp., which is in some cases significant or even severe. The degree of mortality, or absence of mortality, depends on the type of hydrocarbon (crude or refined oils, oil saturated water fractions, PAHs, or refined products) to which the species is exposed, how they are exposed (through oil spills, effluents, the sediment, or food supply e.g. algae), the concentration of the contaminant and the duration of exposure, as well as seasonal influences on the species' condition, especially spawning and reproduction.

Therefore, the 'weight of evidence' based on reported 'severe' (>75%) and 'significant' (25-75%) mortality due to hydrocarbon contamination suggests an overall **'worst case'** resistance assessment of '**None'**. Resilience is probably '**Low**' so sensitivity to petroleum-based oils is assessed as '**High**'. However, it should be noted that the evidence reviewed also documented several occasions in which blue mussels and blue mussel beds had survived significant oiling and most evidence (70% of the articles examined) of exposure to hydrocarbons was reported to result in sub-lethal effects, although it was not clear how detrimental sub-lethal effects or 'stress' is to the species survival. Hence, confidence in the assessments is **'Medium'**.

1.2 *Mytilus* spp. - Transitional metals and organometals

A total of 133 articles were selected from 2,533 articles. These 133 articles focused on the physiological effects of metal exposure on *Mytilus* spp. of which 15 articles focused on the effects of nanoparticulates metals and 18 articles looked at the effects of organometals. The range of 'ranked mortalities'[4] reported in the 133 papers examined is shown in Figure 1.3.

In general, the evidence suggested that longer exposure times were required to understand the true impacts of metal exposure on *Mytilus*, as mussels can close their shells for days. Hence, short-term exposures (e.g. < 48 hrs) may underestimate sensitivity. This agrees with Widdows & Donkin (1992) who suggested that LC_{50} values in *Mytilus* gave a false impression of high tolerance because adult bivalves were able to close their valves and isolate themselves from extreme (potentially lethal) conditions for long periods (i.e. days). Different life stages had different sensitivities. This also agrees with Widdows & Donkin (1992) who noted that adults were >10-fold more sensitive than larvae to copper (Cu), petroleum hydrocarbons and sewage sludge.

However, it was difficult to describe many other general trends in metal toxicity due to the variation in the experimental conditions (e.g. laboratory or field), and especially duration between studies and the different toxicities of the variation metals and their compounds used. Therefore, the results of the review are presented separately for each metal and its compounds.

[4] Mortality is 'ranked' based on the MarESA resistance scale, i.e. some (<25%), significant (25-75%), and severe >75%, and None (observed), with 'sublethal' included as an additional category.

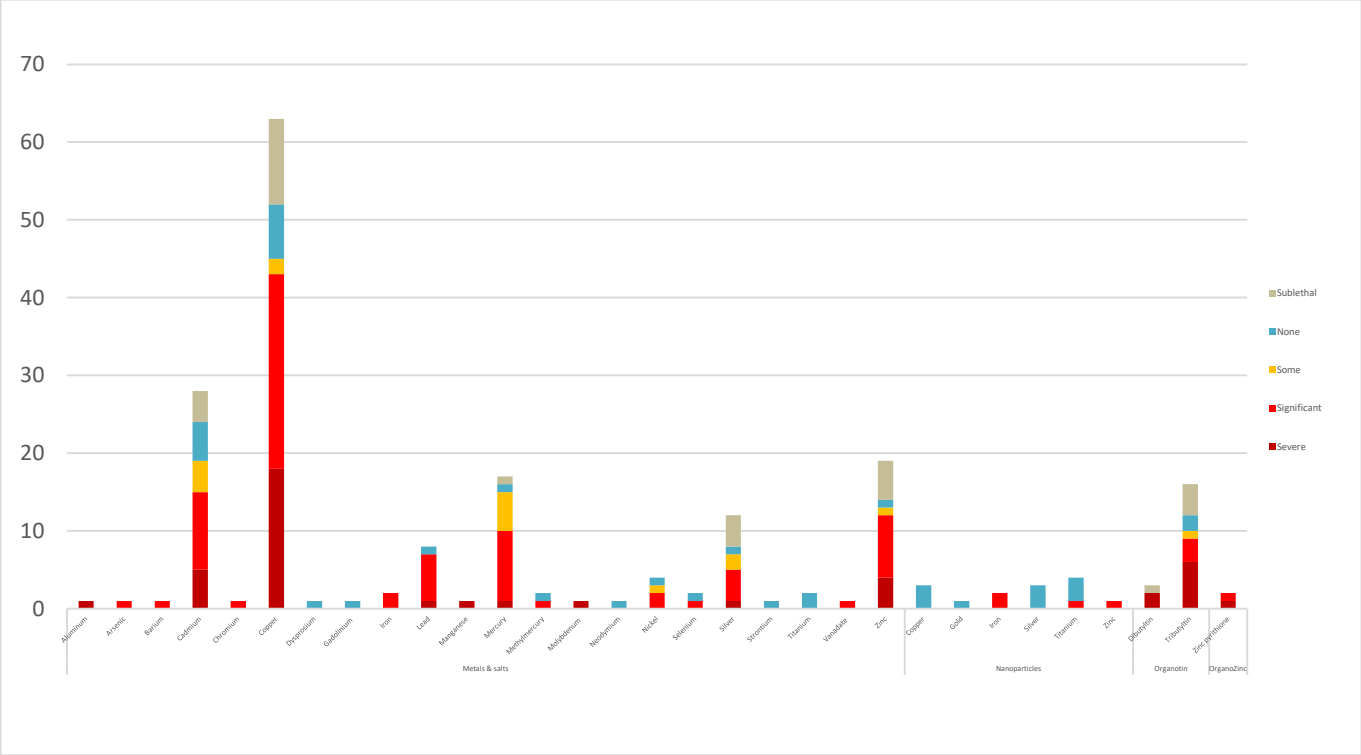

Figure 1.3. Count of ranked mortality (from 'severe' to 'none') in the articles examined for a range of metal contaminants in *Mytilus* spp..

1.2.1 Copper

The effects of copper exposure on *Mytilus* spp. have been well studied with multiple papers investigating the lethality of copper at different concentrations and life stages. A total of 52, of the 133 papers screened, document the lethality of copper, 29 of those looked at the effects on adults, 20 looked at the effects on embryo/larvae stages, and three papers looked at the effects on juveniles (Figure 1.4).

The results from the papers show significant differences in the concentrations at which mortality occurred. The variation in the concentrations that resulted in mortality typically correlated with the exposure duration. For example, Al-subiai *et al.* (2011) observed no mortality of *Mytilus edulis* adults exposed to 50 µg/l (0.05 mg/l) copper for five days. However, Martin (1979) exposed *Mytilus edulis* adults to 50 µg/l (0.05 mg/l) copper for a period of 20 days resulting in complete mortality. The results clearly demonstrate that lower doses of copper can be just as lethal as higher concentrations when the mussels are exposed over a longer period. For example, Martin (1979) exposed groups of *Mytilus edulis* individuals to a variety of concentrations of copper between 0.02 µg/l – 3 µg/l (0.00002 – 0.003 mg/l) for a period of 50 days. Complete mortality occurred at the highest dose within 6 days and at the lowest dose, complete mortality had occurred by day 40.

The development of embryo/larvae life stages of *Mytilus* was shown to be more sensitive to copper than adult stages. Copper has been shown to have toxic effects on the embryo/larvae stages of *Mytilus* development with 100% development abnormality occurring at 10 µg/l with a 48-hour exposure (Yaroslavtseva & Sergeeva, 2007). In *Mytilus californianus,* larval mortality occurred at 6.5 µg/l copper (Hall *et al.,* 2020). In addition, concentrations of copper as low as 0.5 µg/l copper caused the abnormal development of larvae. The experiments showed copper to have dose-dependent effect on embryo-larval development characterized by an increase in abnormal D-larvae with increasing metal concentration (Boukadida *et al.*, 2016).

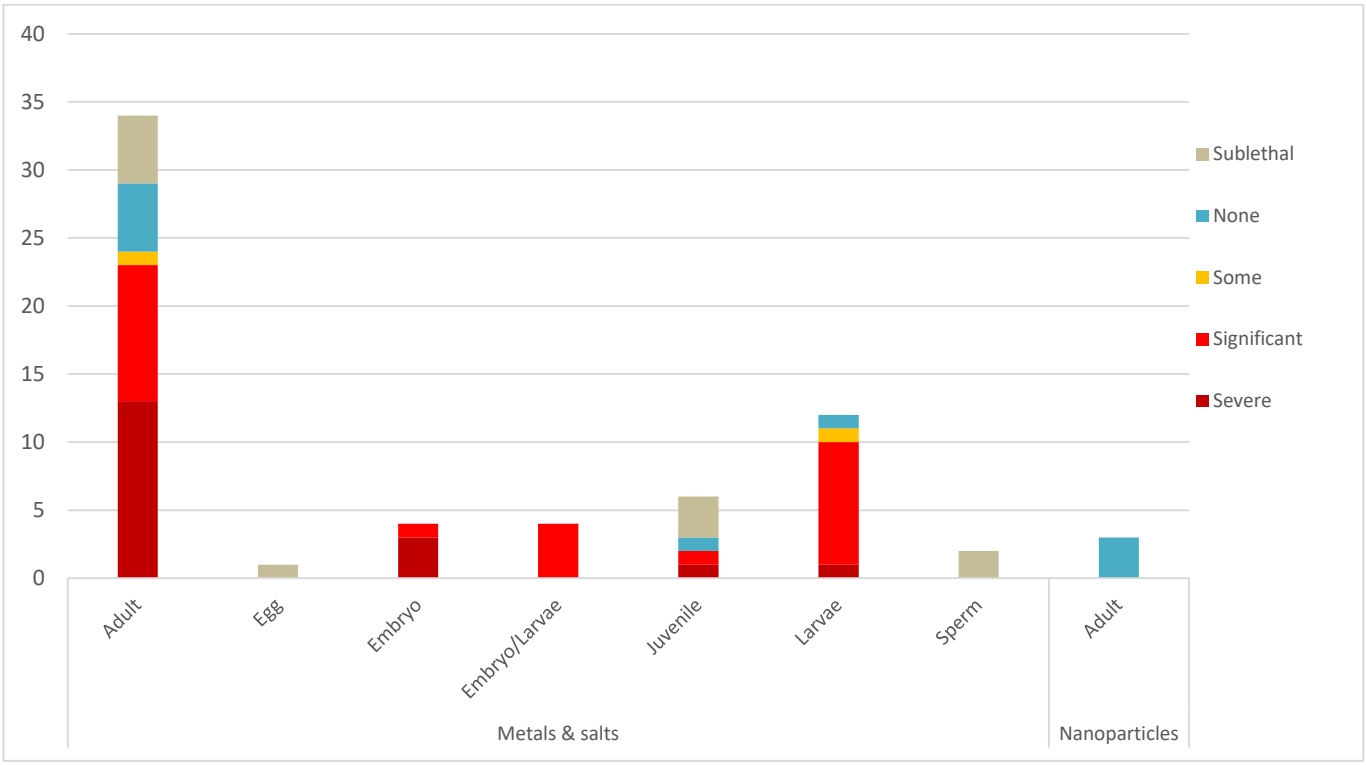

Figure 1.4. Count of ranked mortality (from 'severe' to 'none') in the articles examined for inorganic copper and its compounds in *Mytilus* spp..

1.2.2 Cadmium

Cadmium has the second greatest number of articles reporting lethal effects from exposure, with 24 of 133 screened papers reporting effects on survival. Significant to severe mortality was observed in all life stages of *Mytilus spp*. from exposure to cadmium (Figure 1.5).

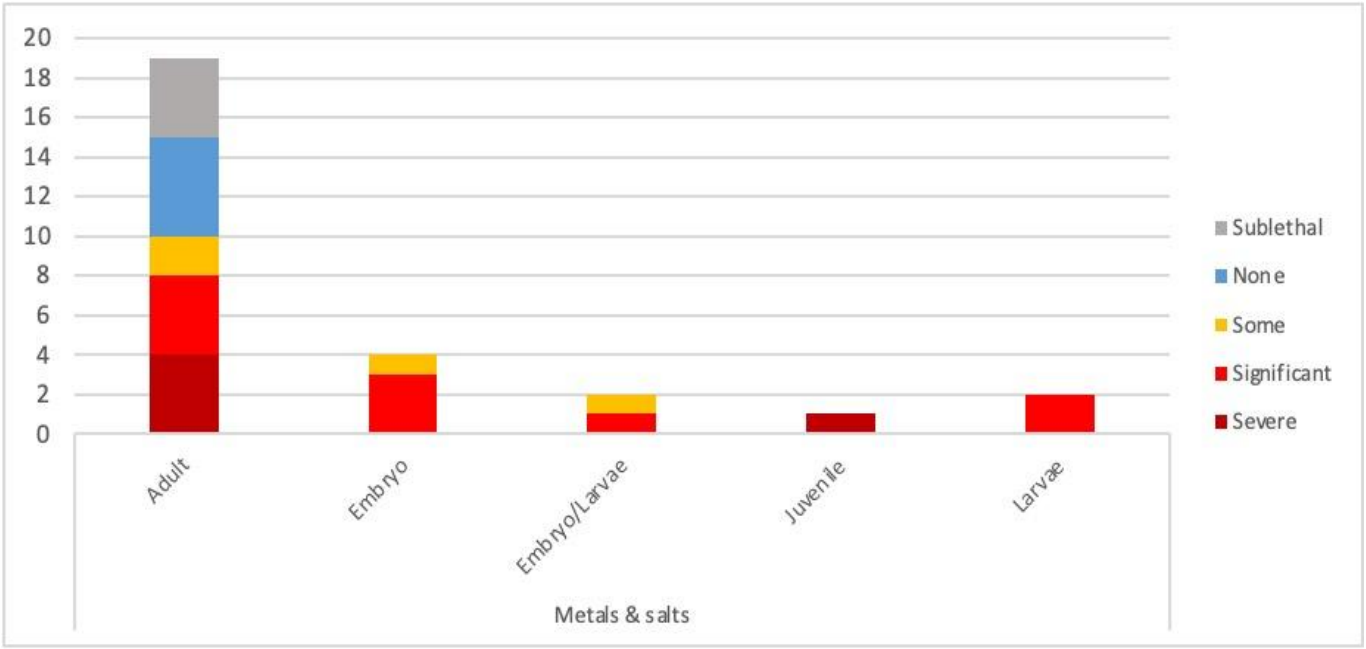

Figure 1.5. Count of ranked mortality (from 'severe' to 'none') in the articles examined for inorganic cadmium and its compounds. (NR= not reported).

The evidence is summarized below.

- Amiard-Triquet (1986) exposed *Mytilus edulis* adults to a large range of concentrations of cadmium over a 16-day period. The cadmium concentration that caused 50% mortality in 96 hours (LC_{50}, 96

hr) was 1550 µg/l (1.55 mg/l). At a concentration of 2500 µg/l (2.5 mg/l) cadmium 100% mortality occurred within 8 days.

- Chalkiadaki *et al.* (2014) exposed *Mytilus galloprovincialis* adults to various concentrations of cadmium (0.5, 1, 2.5 & 20 mg/l) for 20 days with 10 days depuration period. During the experiment, all the mussels exposed to 2.5 mg/l (2500 µg/l) cadmium died within 10 days, and those exposed to 20 mg/l cadmium all died within five days. The mussels exposed to 0.5 and 1 mg/l (500 and 1000 µg/l) cadmium all survived until the end of the experiment with no mortalities.
- Eisler (1971) investigated the acute toxicity of cadmium on a variety of marine organisms including the blue mussel, *Mytilus edulis*. The concentration required to kill half of the population of mussels decreased with time, as follows, 24-hour LC_{50} >200 mg/l; 48-hour LC_{50} 165 mg/l, and 96-hour LC_{50} 25 mg/l.
- Vlahogianni & Valavandis (2007) conducted short-term toxicity tests with cadmium on *Mytilus galloprovincialis* adults establishing a 24-hour LC_{50} of 1700 µg/l (1.7 mg/l) but observing 0% mortality at 100 µg/l (0.1 mg/l).
- Coles *et al.* (1995) found the survival of *Mytilus edulis* adults not to be affected by a seven-day exposure to 40 µg/l and 4 µg/l (0.04 and 0.004 mg/l) cadmium.
- Bebbianno & Langston (1992) found no mortality of *Mytilus galloprovincialis* during a 40-day exposure to cadmium at concentrations of 400 µg/l (0.4 mg/l)
- Bebbianno & Serafim (1998) found no mortality of *Mytilus galloprovincialis* to occur during a 40-day exposure to 100 µg/l (0.1 mg/l) cadmium.
- Talbot *et al.* (1976) determined lethal doses of cadmium exposure on *Mytilus edulis* adults over a period of 200 days. The dose required to cause 50% mortality of the population decreased with increasing exposure time. At 30 mg/l cadmium, 50% mortality occurred within 96 hours, however at a lower concentration of 0.5 mg/l (500 µg/l), 50% mortality occurred within 200 days.
- Myint & Tyler (1982) found cadmium to suppress *Mytilus edulis* gametogenesis at a concentration of 50 µg/l (0.05mg/l) during the early stages of gonad development but did not affect the survival of adults during a 70-day exposure experiment at -1.5 to 0°C, or during a 28-day exposure at 18°C.
- Ahsanullah (1976) determined the acute toxicity of cadmium exposure on *Mytilus edulis* adults, establishing an LC_{50} of 1620 µg/l (1.62 mg/L).
- Nelson *et al.* (1988) exposed *Mytilus edulis* juveniles to cadmium at a variety of concentrations over a 96-hour period to find the lethal concentration; a LC_{50} of 960 µg/l (0.96 mg/l) was established.
- Martin *et al.* (1981) studied the toxicity of cadmium on the embryo development of *Mytilus edulis* and established the 48-hour EC_{50} of cadmium to be 1200 µg/l (1.2 mg/l).
- Beiras & Albentosa (2004) investigated the inhibitory effects of trace metals on the embryos of *Mytilus galloprovincialis*. Cadmium exposure caused an increase in the percentage of abnormal larvae with a dose response effect. A 48-hour EC_{50} 1925 µg/l (1.925 mg/l) cadmium was established, with the lowest observed effect concentration (LOEC) of 500 µg/l (0.5 mg/l).
- Balbi *et al.* (2014) investigated the effects of Cd^{2+} exposure on *Mytilus galloprovincialis*. Adult mussels were exposed to 100 µg/l (0.1 mg/l) for a period of 96 hours, during which time no mortality occurred. Embryo/larvae development was significantly affected by Cd^{2+} inducing a significant decrease in the percentage of normal D-larvae (-41% compared to controls), including larvae held up in the trochophore or pre-veliger stages and malformed larvae.
- Pavicic *et al.* (1994a) observed the toxic effects of cadmium, zinc, and mercury on the development and growth of *Mytilus galloprovincialis* larvae. Mercury was the most toxic followed by zinc and

then cadmium. The combined exposure to zinc and cadmium simultaneously resulted in an antagonistic effect with a higher percentage of normally formed larvae and reduced growth inhibition in comparison to the effects of the metals individually. Cadmium caused significant decreases in growth at concentrations above 2200 µg/l (2.2 mg/l). All three metals caused the abnormal development of veliger larvae with increasing metal concentration causing a higher percentage of abnormal larvae.

- Prato & Biandolino (2007) investigated the toxicity of copper, cadmium, and mercury individually and combined on *Mytilus galloprovincialis* using the embryotoxicity tests. The results showed all the metals to have significant effects on the larval development with the lowest tested concentrations of contaminant causing a significant impact on larvae development. The EC_{50} and LOEC of cadmium were calculated at 21 µg/l (0.021 mg/l) and 6.25 µg/l (0.00625 mg/l), respectively. The toxicity of the metals on larvae development showed an antagonistic effect for each combination of metals.
- Annicchiarico *et al.* (2007) exposed *Mytilus galloprovincialis* larvae to five concentrations of cadmium in the range of 3.125 to 500 µg/l (0.003125 to 0.5 mg/l) to determine the lethal concentration during a 48-hour exposure period. A 48 hr LC_{50} of 590 µg/l (0.59 mg/l) was reported.

1.2.3 Zinc

The effects of zinc exposure on *Mytilus* spp. have been reasonably well studied with 15 articles from the selected 133 articles investigating the lethality of zinc at different concentrations and life stages. Significant mortality has been observed in all life stages of *Mytilus* spp. in these articles (Figure 1.6).

The evidence is summarized below.

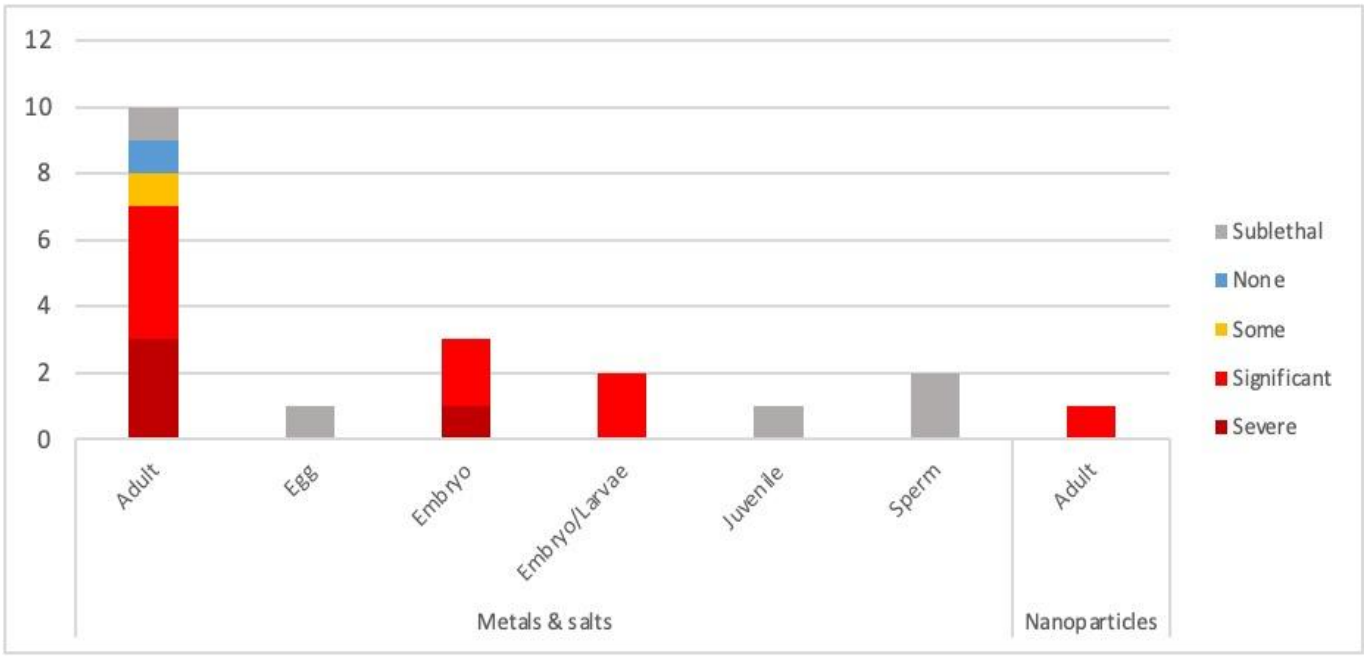

Figure 1.6. Count of ranked mortality (from 'severe' to 'none') in the articles examined for inorganic zinc and its compounds. (NR= not reported).

- D'silva & Kureishy (1978) exposed *Mytilus viridis* to zinc which caused 50% mortality at a concentration of 140 µg/l (0.14 mg/l) and 100% mortality at 250 µg/l (0.25 mg/l) zinc within 48 hours.
- Burbidge *et al.* (1994) found both particulate (elemental) Zinc and soluble Zinc ($ZnCl_2$) to be lethal to *Mytilus edulis* at 10 µg/l (0.01 mg/l) causing 100% mortality after 12 days. At concentrations of 2 µg/l (0.002 mg/l) particulate zinc did not cause any mortalities during the 12-day period; however, soluble zinc did cause some mortalities.

- Amiard-Triquet (1986) exposed mussels to a large range of concentrations of zinc over a 16-day period. The concentration of zinc that caused 50% mortality in 96 hours (LC_{50}) was >5000 µg/l (>5 mg/l). Complete (100%) mortality occurred after 16 days at 5000 µg/l (5 mg/l) zinc.
- Abel (1976) investigated the effects of pollutants on the filtration rate of *Mytilus edulis*. A reduction in filtration rates occurred with increasing concentrations of zinc. The LC_{50} was estimated to be 7,800 µg/l (7.8 mg/l) after 96 hours.
- Hietanen *et al.* (1988) found the LC_{50} value of zinc on *Mytilus edulis* to be 20.8 mg/l during a 41-day exposure. Throughout the experiment, the LC_{50} value changed in relation to time with lower concentrations causing the same percentage of mortalities as higher concentrations over a longer period.
- Cotter *et al.* (1982) investigated the effects of zinc on the survival of *Mytilus edulis* at different temperatures and salinities. The results showed zinc to cause mortality at a faster rate at 22°C and 35% salinity, than at lower temperatures and salinities.
- Myint & Tyler (1982) found no mortalities of *Mytilus edulis* adults occurred during a 70-day exposure to 200 µg/l (0.2 mg/l) zinc at -1.5 to 0°C, or during a 28-day exposure at 18°C.
- Nadella *et al.* (2009) assessed the embryo-larvae toxicity of zinc on mussel *Mytilus trossulus* during a 48-hour development test. Zinc caused abnormal larvae development with an established EC_{50} of 150 µg/l (0.15 mg/l) and an EC_{20} of 99 µg/l (0.099 mg/l).
- Martin *et al.* (1981) tested the toxicity of zinc on the embryos of *Mytilus edulis*. A 48-hour EC_{50} value of 175 µg/l (0.175mg/l) zinc was established for abnormal development.
- Beiras & Albentosa (2004) investigated the inhibitory effects of trace metals on the embryos of *Mytilus galloprovincialis*. Zinc exposure caused an increase in the percentage of abnormal larvae with a dose response effect. A 48-hour EC_{50} between 160-320 µg/l (0.16-0.32 mg/l) zinc was established.
- Pavicic *et al.* (1994b) observed the toxic effects of zinc on the development and growth of *Mytilus galloprovincialis* larvae. Zinc exposure caused abnormal development of veliger larvae with increasing metal concentration causing a higher percentage of abnormal larvae. A 48-hour EC_{50} of 145 µg/l (0.145mg/l) zinc was established.
- Ahsanullah (1976) determined the acute toxicity of zinc exposure on *Mytilus edulis* adults, establishing an LC_{50} of 2500 µg/l (2.5 mg/l) zinc in static exposure trials, and LC_{50}s of 3600 & 4300 µg/l (3.6 & 4.3 mg/l) in flow through exposure trials.

1.2.4 Mercury

The effects of mercury toxicity on *Mytilus* spp. have been assessed in several scientific articles. Severe mortality has been reported in juvenile mussels, and significant mortality has been reported in adult and embryo/larvae life stages (Figure 1.7).

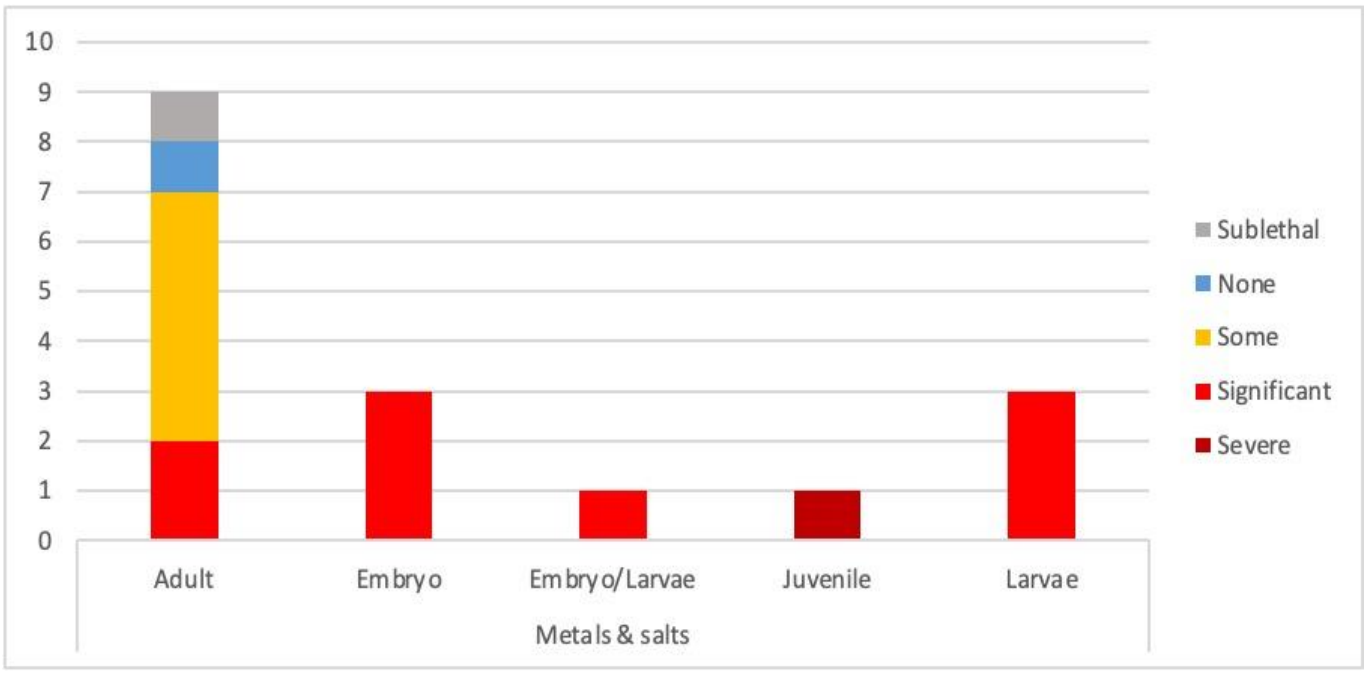

Figure 1.7. Count of ranked mortality (from 'severe' to 'none') in the articles examined for inorganic mercury and its compounds.

- Micallef & Tyler (1990) found that exposure of *Mytilus edulis* to 50 µg/l (0.05mg/l) mercury for five days did not affect survival during that period. However, Micallef & Tyler (1978) found mercury at concentrations of 2500 µg/l (2.5 mg/l) to cause 50% population mortality of *Mytilus edulis* within 96 hours. A long-term 98-day study by Domouhtsidou & Dimitriadis (2000) observed a concentration of 100 µg/l (0.1 mg/l) mercury to cause significant mortality (54.2%) of adult *Mytilus galloprovincialis*.
- Nelson *et al.* (1988) exposed *Mytilus edulis* juveniles to mercury at a variety of concentrations over a 96-hour period to find the lethal concentration. The established LC_{50} and LC_{95} were 161 µg/l (0.161 mg/l) and 284 µg/l (0.284mg/l) respectively.
- Martin *et al.* (1981) studied the toxicity of mercury on the embryo development of *Mytilus edulis* and established the 48-hour EC_{50} of mercury to be 5.8 µg/l (0.0058 mg/l).
- Beiras & His (1995) investigated the effects of mercury on *Mytilus galloprovincialis* embryos and the growth and survival of larvae at different stages of development. Larval growth was significantly reduced at 4 µg/l (0.004mg/l) mercury and an EC_{50} of 10 µg/l (0.01 mg/l) mercury was established for abnormal growth. Embryos were more sensitive to mercury exposure than the larvae with an EC_{50} of 10 µg/l (0.01 mg/l). The results showed the D-shaped larval stage to be the most sensitive larval stage, followed by early umbonate, late umbonate and then eyed larvae stage, with LC_{50}s of 51, 164, 322, 383 µg/l (0.051, 0.164, 0.322 and 0.383 mg/l) respectively.
- Beiras & Albentosa (2004) investigated the inhibitory effects of mercury on the embryo development of *Mytilus galloprovincialis*, establishing a 48-hour EC_{50} of 2 µg/l (0.002 mg/l).
- Pavicic *et al.* (1994) observed the toxic effects of mercury on the development and growth of *Mytilus galloprovincialis* larvae. Mercury exposure caused the abnormal development of veliger larvae with increasing concentration causing a higher percentage of abnormal larvae. The established 48-hour EC_{50} for mercury was 3.5 µg/l (0.0035mg/l).
- Prato & Biandolino (2007) investigated the toxicity of mercury on *Mytilus galloprovincialis* development using the embryotoxicity test. The results showed mercury to have significant effects on larval development. The lowest tested concentration of 0.4 µg/l (0.0004mg/l) mercury caused a significant impact on larvae development; and the 48-hour EC_{50} was established at 1 µg/l (0.001 mg/l).

- Annicchiarico *et al.* (2007) exposed *Mytilus galloprovincialis* larvae to five concentrations of mercury in the range of 6.25-100 µg/l (0.00625–0.1 mg/l) to determine the lethal concentration during a 48-hour exposure period; an LC_{50} of 10 µg/l (0.01 mg/l) was established.
- The toxicity of methylmercury exposure on *Mytilus edulis* was monitored in two research papers. Dorn (1976) exposed mussels to concentrations of methylmercury acetate between 400 and 2800 µg/l (0.4 and 2.8 mg/l) during a 48-hour period and reported that the feeding rate of *Mytilus edulis* decreased in response to increasing concentration. However, no significant mortalities were recorded during the 48-hour exposure period. Pelletier (1988) exposed *Mytilus edulis* to methylmercury complexes at concentrations of 3 µg/l for 32 days and reported significant mortalities of 30-67%.

1.2.5 Silver

The effects of silver toxicity on *Mytilus* spp. have been assessed in several articles. Severe mortality was observed in juvenile mussels, and significant mortality was reported in adults and embryo/larvae life stages (Figure 1.8).

- Boukadida *et al.* (2016) investigated the toxic effects of silver concentrations (0.1, 1, 3, 10, 30 µg/l) on *Mytilus galloprovincialis* larvae development at different temperatures (18, 20, 22 or 24°C). The results showed a dose-dependent effect on embryo-larval development characterized by an increase in the rate of abnormal D-larvae with increasing silver concentration. Significant embryotoxicity was observed at the lowest tested concentration of silver (0.1 µg/l) with 19.7% of abnormal D-larvae. At 30 µg/l of silver, there was 100% larval abnormality. The 48-hour EC_{50} for silver at 18°C of was calculated at 6.58 µg/l.
- Metayer *et al.* (1990) observed the toxicity of silver on *Mytilus galloprovincialis* adults at three different concentrations. For each of the tested concentrations 1-10, 100 and 1000 µg/l (0.001-0.01, 0.1, and 1 mg/l) LT_{50} values were calculated. At the highest concentration of 1000 µg/l (1 mg/l), 50% mortality occurred at 3.3 days, at 100 µg/l (0.1 mg/l) silver 50% mortality occurred at 4.6 days and at 1 µg/l (0.001mg/l) 50% mortality was >16 days.
- Berthet *et al.* (1992) observed no mortality (0%) in adult *Mytilus galloprovincialis* after exposure to 20 µg/l silver for 28 days.
- A long-term 98-day study by Domouhtsidou & Dimitriadis (2000) found a concentration of 100 µg/l (0.1 mg/l) silver to cause significant mortality (51.4%) of adult *Mytilus galloprovincialis*.
- Nelson *et al.* (1988) exposed *Mytilus edulis* juveniles to silver at a variety of concentrations over a 96-hour period to find the lethal concentrations and determined a LC_{50} of 159 µg/l (0.159mg/l) silver.
- Martin *et al.* (1981) studied the toxicity of silver on the embryo development of *Mytilus edulis* and established the 48-hour EC_{50} of 14 µg/l (0.014 mg/l) silver.

1.2.6 Lead

The effects of lead exposure on *Mytilus* spp. has been studied by multiple papers. The lethal effects of lead were reported in most of the articles examined, although not all the papers reported direct mortalities. Abnormal larval development has been included as a lethal effect as abnormal development may be expected to lead to recruitment failure and population decline. There was an almost 50/50 split in the papers that assessed the toxicity of lead on adult mussels or on early larvae development stages (Figure 1.9).

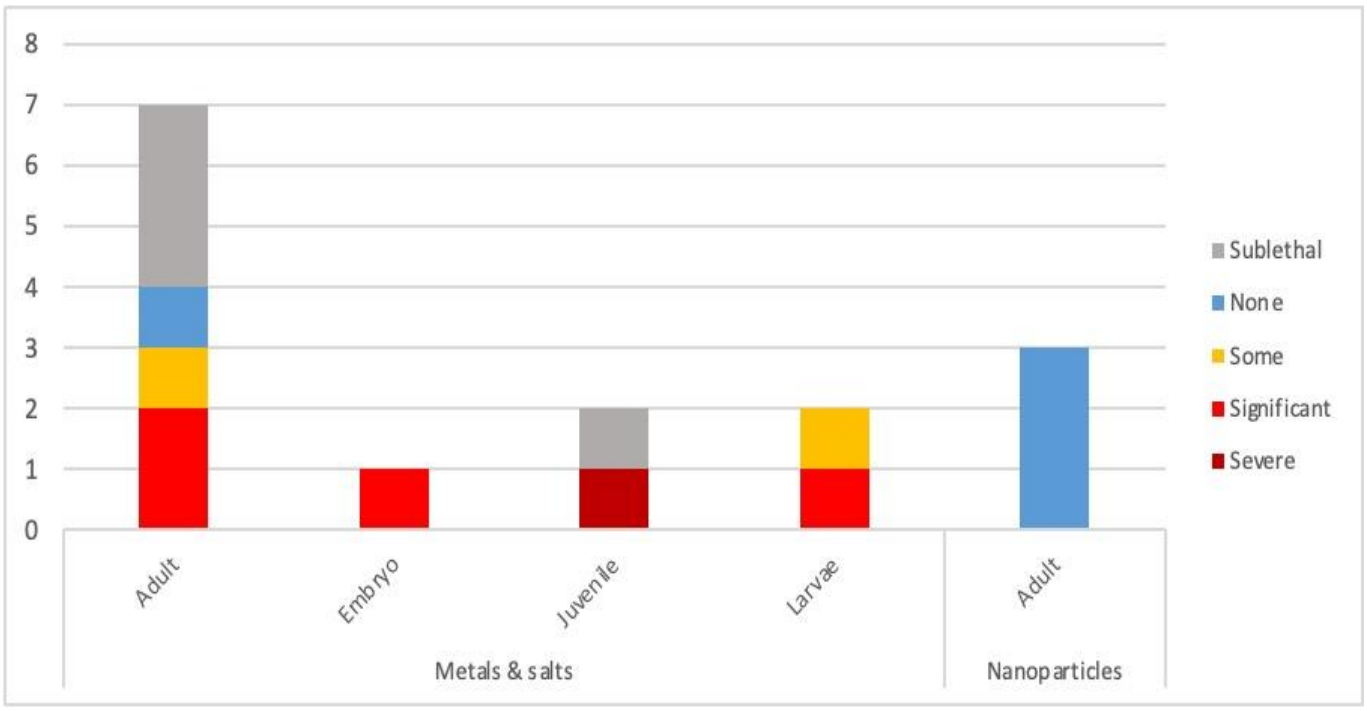

Figure 1.8. Count of ranked mortality (from 'severe' to 'none') in the articles examined for inorganic silver and its compounds.

Adults

- Freitas *et al.* (2019) observed no mortalities from exposure of *Mytilus galloprovincialis* to 50 µg/l (0.05mg/l) lead at a variety of temperatures and salinities for a period of 28 days.
- Vlahogianni & Valavandis (2007) conducted short term lead toxicity tests on *Mytilus galloprovincialis* over 24 hours and 10 days. The observed concentration required to cause mortality in 50% of the test population during a 24-hour exposure was calculated as LC_{50} 4500 µg/l (4.5 mg/l) lead. Additionally, Vlahogianni & Valavandis (2007) observed no mortalities to occur during a 10-day exposure to 150 µg/l (0.15 mg/l) lead.
- However, a long-term study by Domouhtsidou & Dimitriadis (2000) found a lower concentration of 100 µg/l (0.1 mg/l) lead to cause significant mortality (48.5%) of *Mytilus galloprovincialis* during 98-day exposure trials.
- Talbot *et al.* (1976) determined the lethal dose of lead on *Mytilus edulis* adults during a long-term exposure experiment. Talbot *et al.* (1976) observed a clear correlation in the exposure duration and concentration required to cause mortality to 50% of the test population, as follows: LD_{50} 20 mg/l 40 days; LD_{50} 30 mg/l 30-40 days; LD_{50} 10-20 mg/l 50-100 days; and LD_{50} 10 mg/l 100-200 days. The results showed that the lethality of lead depends on the exposure concentration and exposure duration

Embryo/larvae

The results from the examined papers have shown that *Mytilus* embryos and larvae are more sensitive to lead exposure than adult specimens.

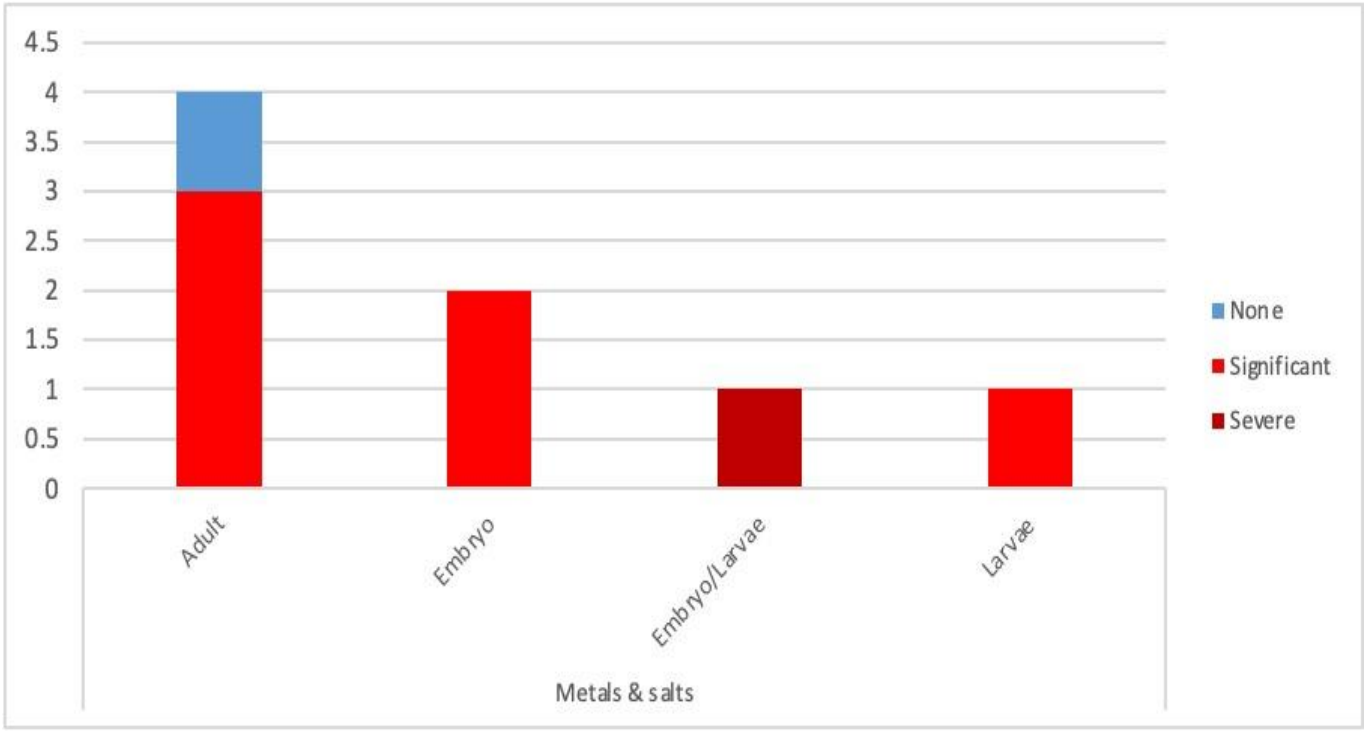

Figure 1.9. Count of ranked mortality (from 'severe' to 'none') in the articles examined for inorganic lead and its compounds.

- Hrs-Brenko *et al.* (1977) investigated the effects of different concentrations of lead at different salinities and temperatures on embryo development of *Mytilus galloprovincialis*. The embryonic development of *Mytilus galloprovincialis* was inhibited depending on the salinity and temperature. The percentage of embryonic development two days after fertilization decreased with increasing concentrations of lead. Lead exposure caused undeveloped larvae, abnormal larvae, and mortality of larvae with the percentage of effect depending on concentration, exposure time, temperature, and salinity. During the first 48 hours of exposure, the mortality rate of the larvae at all concentrations was very low, however, after 96 hours, the mortality rate had significantly increased, as follows:
    - at 100 µg/l (0.1 mg/l) lead embryo development ranged between 8.86-95.60%;
    - at 250 µg/l (0.25 mg/l) lead embryo development ranged between 0-87%;
    - at 500 µg/l (0.5 mg/l) lead embryo development ranged between 0-46.54%; and
    - at 1000 µg/l (1 mg/l) lead embryo development ranged between 0-22.36%.
- Lussier *et al.* (1999) observed 476 µg/l (0.476 mg/l) lead to cause a 50% reduction in larvae hatch rates. Similarly, Martin *et al.* (1981) reported 50% of *Mytilus edulis* larvae to have abnormal development when exposed for 48 hours to 476 µg/l lead. In addition, Beiras & Albentosa (2004) investigated the inhibitory effects of lead on the embryos of *Mytilus galloprovincialis* and established a 48-hour EC_{50} of 221 µg/l (0.221mg/l).

1.2.7 Nickel

The effects of nickel on *Mytilus* spp. have been investigated by a limited number of papers.

- Stromgren *et al.* (1982) observed concentrations up to 200 µg/l (0.2mg/l) nickel did not significantly affect the behaviour or growth rate of *Mytilus edulis* when compared to the control.

- Nadella *et al.* (2009) assessed the embryo-larvae toxicity of nickel on mussel *Mytilus trossulus* during a 48-hour development test. Nickel caused abnormal larvae development with an established EC_{50} of 150 µg/l (0.15mg/l) and an EC_{20} of 82 µg/l (0.082 mg/l).
- Martin *et al.* (1981) investigated the effects of nickel on *Mytilus edulis* larvae development during a 48-hour experiment, and established the 48-hour EC_{50} of nickel to be 891 µg/l (0.891 mg/l).
- Chalkiadaki *et al.* (2014) exposed *Mytilus galloprovincialis* adults to various concentrations of nickel (0.5, 1, 2.5 & 20 mg/l) for 20 days with 10 days depuration period. No mortalities occurred during the exposure period even at the highest concentration of 20 mg/l nickel.
- Deforest & Schlekat (2013) reviewed species sensitivity of chronic nickel toxicity. The toxicity of nickel on *Mytilus galloprovincialis* larval development was conducted by exposing embryos to nickel in static 48-hour toxicity tests. Four tests were conducted using natural seawater collected from four different locations with dissolved organic carbon (DOC) concentrations between 12,000 µg/l (1.2 mg/l) and 2700 µg/l (2.7 mg/l) and salinities between 29.5 and 30.1‰. The EC_{10}s (259, 228, 256 & 350 µg/l nickel) were based on normal larval shell development. The results showed no clear differences in the toxicity of nickel depending on DOC or salinity.

1.2.8 Titanium

Only two research papers investigated the effects of titanium exposure on *Mytilus* spp. Monteiro *et al.* (2019a&b) found titanium at concentrations below 100 µg/l (0.1 mg/l) to not significantly impact the survival of *Mytilus galloprovincialis* adults, during 14-day exposures.

1.2.9 Iron

Three research papers investigated the effects of iron on *Mytilus* spp.

- Kadar *et al.* (2010) found soluble Fe at concentrations of 0.08, 0.8, and 8 mg/l did not affect the development of *Mytilus galloprovincialis* larvae significantly in natural seawater at pH 8.1 during a 48-hour exposure. However, at pH 7 and pH 6 the percentage of normally developed D-shelled larvae reduced drastically, and the percentage of delayed embryos increased.
- Vlahogianni & Valavandis (2007) conducted short-term 24-hour toxicity exposure of *Mytilus galloprovincialis* adults to 1, 4, 6, 8, and 10 mg/l iron. A 24-hour LC_{50} value of >6 mg/l iron was established. In addition, no mortality occurred during a 10-day exposure to 0.15 mg/l iron.
- Pagano *et al.* (1996) studied the toxicity of iron on the early development, fertilization, and offspring quality of *Mytilus galloprovincialis*. Pagano *et al.* (1996) observed severe embryotoxicity when mussel embryos were reared in Fe (III) at concentrations above 10^{-6} M. At the highest tested concentration of iron 10^{-4} M, 25% larvae abnormality occurred. Iron exposure did not affect the fertilization success of sperm or cause a significant increase in the percentage of abnormal larvae following sperm exposure to iron.

1.2.10 Selenium

The toxicity of selenium on *Mytilus* spp. was examined in two research papers. Martin *et al.* (1981) investigated the effects of selenium on *Mytilus edulis* larvae development, establishing the 48-hour EC_{50} to cause abnormal larvae development of selenium to be >10 mg/l. Micallef & Tyler (1990) investigated the effects of selenium on *Mytilus edulis* adults, and reported no mortality after exposure to 50 µg/l selenium during a five-day exposure period. However, significant reductions in filtration rates of *Mytilus edulis* were observed.

1.2.11 Other metals

Aluminium Pagano *et al.* (1996) studied the toxicity of aluminium on the early development, fertilization, and offspring quality of *Mytilus galloprovincialis*. Pagano *et al.* (1996) found severe embryotoxicity when mussel embryos were reared in $Al_2(SO_4)_3$ at concentrations $\geq 10^{-6}$M. At a concentration of $3x10^{-6}$ M, most larvae developed abnormally with only 2 to 4% normal D-larvae development. At concentrations between 10^{-5} and 10^{-4} M only abnormal larvae developed. Aluminium exposure did not affect fertilization success or cause a significant increase in the percentage of abnormal larvae following sperm exposure to aluminium, except for the 10^{-4} M treatment group.

Arsenic. Martin *et al.* (1981) established the 48-hour EC_{50} of arsenic causing abnormal embryo development to be >3 mg/l.

Barium. Spangenberg & Cherr (1996) investigated the impacts of barium on the development of *Mytilus californianus* embryos and larvae. Barium significantly affected the development of larvae at concentrations between 200 & 800 µg/l (0.2 & 0.8 mg/l), causing abnormal and delayed development following 48 hours of exposure to barium. The NOEC determined was 0.1 mg/l barium and the EC_{50} was determined at 1890 µg/l (1.89 mg/l) barium.

Chromium. Martin *et al.* (1981) established the 48-hour EC_{50} of chromium causing abnormal embryo development to be 4469 µg/l (4.469 mg/l).

Dysprosium. Freitas *et al.* (2020a) found 28-day exposures to a variety of concentrations of dysprosium up to 40 µg/l (0.04 mg/l) did not affect the survival of *Mytilus galloprovincialis.* However, metabolic and oxidative effects did occur.

Gadolinium. Henriques *et al.* (2019) found concentrations of gadolinium up to 120 µg/l (0.12 mg/l) not to affect the survival of *Mytilus galloprovincialis* during a 28-day study. However, exposure to gadolinium did affect the biochemical performance of *Mytilus galloprovincialis*.

Manganese. Morgan *et al.* (1986) found the metal manganese to cause abnormal *Mytilus* larvae development and cause mortality during a 48-hour exposure period. The larvae were exposed to concentrations between 1 and 560 mg/l and an EC_{50} of 30 mg/l manganese was established. At 320 mg/l, 100% of larvae developed abnormally and survival was 1%. At the highest tested concentration of 560 mg/l 100% larval mortality occurred.

Molybdenum. Morgan *et al.* (1986) found the metal molybdenum to cause abnormal *Mytilus* larvae development and caused mortality during a 48-hour exposure period. The larvae were exposed to concentrations between 1 and 560 mg/l and an EC_{50} of 147 mg/l molybdenum was established. At 320 mg/l, 76.9% of larvae developed abnormally and survival was 7%. At the highest tested concentration of 560 mg/l, survival was 1% and 100% larvae abnormality occurred.

Neodymium. The survival of *Mytilus galloprovincialis* was not affected when exposed to a variety of concentrations of neodymium up to 40 µg/l (0.04 mg/l) for a period of 28 days (Freitas *et al.*, 2020b).

Strontium. Spangenberg & Cherr (1996) investigated the impacts of strontium on the development of *Mytilus californianus* embryos and larvae. Strontium did not affect the development of larvae at concentrations up to 20 mg/l.

Vanadium. Miramand & Unsal (1978) found an exposure concentration of 6500 µg/l (6.5 mg/l) vanadate to cause 50% mortality of *Mytilus galloprovincialis* within nine days of exposure.

1.2.12 Organometals

Tributyltin. The effects of tributyltin exposure on the survival of *Mytilus* spp. were investigated by multiple research papers.

- Guolan & Young (1995b) observed the effects of 60 days exposure to tributyltin chloride on *Mytilus edulis*. The results showed that exposure concentrations between 0.02 and 0.05 µg/l TBT did not affect the survival of the mussels during the 60-day period.
- Beiras & Bellas (2008) investigated the effect of TBT on the inhibition of embryo development of *Mytilus galloprovincialis*, using the percentage of normal larvae as the end point. The lowest observed effect concentration (LOEC) and the concentration that caused a 10% reduction in the percentage of morphologically normal larvae was 0.2 µg/l TBT, and the concentrations that caused a 50% reduction in the percentage of morphologically normal larvae was 0.377 µg/l TBT.
- Stenalt *et al.* (1998) studied the effects of tributyltin on *Mytilus edulis* larvae and post larvae over a 15-day period. The effects of TBT on mortality, growth, and settlement were assessed. The mortality of larvae increased in response to increasing TBT concentration, with an established LC_{50} of 0.254 µg/l.
- Lapota *et al.* (1993) found tributyltin to affect the growth and survival of *Mytilus edulis* larvae. The survival of larvae exposed to TBT ranged between 52 to 58%. The survival for the 0.006, 0.05, and 0.13 µg/l treatments were 80, 86 and 65%, respectively. By day 33, the mean survival had decreased to 58% in 0.006 mg/l treatment and 52% in the 0.05 and 0.13 µg/l treatments.
- Mazzei *et al.* (2015) tested the toxicity of TBT on the motility of *Mytilus galloprovincialis* sperm. The results showed dose-dependent sperm motility alteration, with the lowest tested concentrations of 0.0001 mg/l (0.1 µg/l) causing reductions in motility. At concentrations between 0.001-1000mg/l, the motility of the sperm was completely inhibited within 60 minutes. In addition, the exposure to TBT caused changes in sperm morphology with the sperm tail forming a hook shape.
- Beaumont & Budd (1984) investigated the effects of tributyltin on the mortality of *Mytilus edulis*. The results showed low concentrations of TBT to be lethal to larvae, with concentrations of TBT (0.1 µg/l) found in the natural environment to cause 50% mortality rates within 15 days and to cause surviving larvae to be moribund and grow significantly more slowly than the controls.
- Salazar *et al.* (1987) ran two test groups exposing *Mytilus edulis* juvenile to six different concentrations of TBT (0.04, 0.05, 0.07, 0.08, 0.16, and 0.2 µg/l) over a period of 56 and 196 days. None of the treatments affected the survival of the mussels during the trial period.
- Salazar & Salazar (1989) tested the impacts of different concentrations of TBTO on *Mytilus edulis*. At a concentration of 3 µg/l TBTO mortality did not occur during the 10-day trial period. However, at a concentration of 76 µg/l TBTO 100% mortality occurred within seven days.
- Jha *et al.* (2000) found tributyltin oxide concentrations between 0.56 and 5.65 µg/l to be toxic to the embryo-larval stages of *Mytilus edulis*, causing mortality and abnormal development with increased concentration causing increased mortality/abnormality.
- Dixon & Prosser (1986) observed clear evidence of dose-dependent reduction in survival for mussel larvae exposed to TBTO. *Mytilus edulis* larvae were exposed to 0.05, 0.1, 0.5, 1, and 5 µg/l TBTO for a period of 96 hours, during which time 14, 44, 54, 79 and 97% mortality occurred, respectively.
- Valkirs *et al.* (1987) monitored the mortality of *Mytilus edulis* over a period of 66 days to establish a reliable LC_{50} value. The results of the exposure treatment produced an LC_{50} of 0.97 µg/l TBT, which is considerably lower than 96-hour LC_{50} data reported in literature for this species and contaminant. Valkirs *et al.* (1987) stated the importance of long-term bioassay testing for assessment of realistic environmental toxicity levels, particularly with slow-acting toxicant such as tributyltin.

Dibutyltin. The effects of dibutyltin exposure on the survival of *Mytilus* spp. were investigated by two research papers. Lapota *et al.* (1993) observed dibutyltin exposures to affect the growth and survival of *Mytilus edulis* larvae. The survival of the larvae in the 2, 20, and 200 µg/l treatments were 88, 85, and

62% respectively. By day 33, survival rates were 83% in 2 µg/l treatment, 76% in the 20 µg/l treatment and 1% in the 200 µg/l treatment.

Mazzei *et al.* (2015) tested the toxicity of DBT on the motility of *Mytilus galloprovincialis* sperm. The results showed dose-dependent sperm motility alteration, with the lowest tested concentrations of 0.0001 mg/l (0.1 µg/l) causing reductions in motility. At concentrations between 0.001-1000 mg/l, the motility of the sperm was completely inhibited within 60 minutes. In addition, the exposure to DBT caused changes in sperm morphology with the sperm tail forming a hook shape.

Zinc pyrithione is an organometal that is used as an anti-fouling agent. The toxicity of zinc pyrithione on *Mytilus edulis* was investigated by two papers at two different life stages. Avelelas *et al.* (2017) investigated the effects of zinc pyrithione on adult mussels and reported a 96-hour LC_{50} at 211.3 µg/l (0.21 mg/l) while complete mortality occurred at 500 and 1000 µg/l (0.5 and 1 mg/l).

Bellas *et al.* (2005) investigated the effects of zinc pyrithione on the development of *Mytilus edulis* larvae, finding significant toxicity effects on the embryonic development at low concentrations 3.6 nM (EC_{10}). Normal development was found to be completely inhibited at 24 nM and the concentration required to cause 50% abnormal larvae development was calculated at 8 nM (48-hour EC_{50}).

1.2.13 Nanoparticulate metals

Titanium nanoparticulates. Four papers investigated the effects of nanoparticulate titanium on *Mytilus* spp. Balbi *et al.* (2014) exposed *Mytilus galloprovincialis* adults to 0.1 mg/l n-TiO_2 for a period of 96 hours, during which time no mortality occurred. Similarly, Canesi *et al.* (2014) exposed *Mytilus galloprovincialis* adults to 0.1 mg/l n-TiO2 for a period of 24 hours, during which time no mortality occurred. Also, Canesi *et al.* (2010) found exposure concentrations between 0.05-5 mg/l nano-titanium not to affect the survival of *Mytilus galloprovincialis* adults during a 24-hour exposure period.

Balbi *et al.* (2014) observed the effects of n-TiO_2 on larval development. Larvae were exposed to n-TiO2 for 48 hours, which did not significantly affect larval development. However, Libralato *et al.* (2013) observed titanium (n-TiO_2) exposure to cause embryotoxicity to *Mytilus galloprovincialis*, producing abnormal larvae. Titanium dioxide was tested at concentrations between 0.5-64 mg/l in light and dark exposure conditions. The results from the experiment showed non-linear regression producing two EC_{50} values per exposure. The maximum ecotoxicological effects were detected at 4 and 8 mg/l. The lowest observed effects were detected at 0.5 mg/l.

Zinc oxide nanoparticulates. Hanna *et al.* (2013) exposed *Mytilus galloprovincialis* adults to nanoparticulate zinc oxide for a period of 12 weeks. The mussels were split into size groups and exposed to 0.1, 0.5, 1, and 2 mg/l Zinc. The mean survival of the mussels in the control group was similar to the large and small mussel groups at all concentrations, except for the groups at the highest exposure concentration. After six weeks of exposure to 2 mg/l zinc large mussels had 91% survival and small mussels had 59% survival, but after 12 weeks of exposure, survival was down to 62% in the large group and 23% in the small group.

Copper oxide nanoparticulates. The effects of copper oxide nanoparticles were investigated in five articles. The survival of *Mytilus galloprovincialis* was not influenced when exposed to 0.01 mg/l copper oxide over 15-day periods (Gomes *et al*., 2011; Gomes *et al*., 2012; Gomes *et al*., 2013b; Gomes *et al*., 2014a). In addition, Hu *et al*. (2014) found that concentrations between 0.4 – 1 mg/l copper oxide nanoparticles did not affect the survival of *Mytilus edulis* during a one-hour exposure.

Iron oxide nanoparticulates. The effects of iron nanoparticles were investigated in two articles. Kadar *et al.* (2010) found neither nano-Fe nor soluble Fe concentrations to affect the development of *Mytilus* larvae significantly in natural seawater at pH 8.1. However, at pH 7 and pH 6, the percentage of normally developed D shelled larvae drastically reduced, and the percentage of delayed embryos increased. Furthermore, Kadar *et al.* (2011) found sperm exposure to zero-valent iron to affect the

development of *Mytilus* larvae significantly, indicated by the decrease in normal D-larvae. At the highest tested concentration of 10 mg/l, D-larvae were reduced to below 40%. In addition, sperm fertility was reduced by zero-valent iron exposure.

Gold nanoparticulates. Tedesco *et al.* (2010) exposed *Mytilus edulis* adults to nanoparticulate gold for a 24-hour period. No mortality occurred during the 24-hour period.

Silver nanoparticulates. The survival of *Mytilus galloprovincialis* adults was not influenced by exposures to 0.01 mg/l silver nanoparticles over 15-day periods (Gomes *et al.,* 2013a&b; Gomes *et al.,* 2014b).

1.2.14 Sensitivity assessment – Transitional metals and organometals

The number of articles that report mortalities due to metal, organometals, and nanoparticulate metals in *Mytilus* spp. are *summarized* in Figure 1.3 and in Table 1.3 and Table 1.4 below. Relevant resistance ranks and resultant sensitivities are shown in Table 1.3 and Table 1.4 based on the weight of evidence and 'worst-case' approach outlined above.

The majority of the evidence examined copper, followed by cadmium, zinc, silver, and mercury (Figure 1.3; Table 1.3). The evidence suggests that *Mytilus* adults and juveniles have a **'High'** sensitivity to copper, cadmium, mercury and silver and a **'Medium'** sensitivity to iron, lead, methylmercury and neodymium. The confidence in those assessments is probably **'Medium'** due to the volume of evidence examined. However, it is also clear that there is considerable variation in response to metal exposure, due in part to the variation in the experimental studies, and especially the concentration and exposure duration used.

Less evidence for the remaining metals and especially the organometals and nanoparticulate metals was found, and in some cases, the sensitivity assessment is based on one or two papers (e.g. nanoparticulate Zinc, or tributyltin oxide). While the articles present are all 'High' to 'Medium' quality and directly applicable, it may be prudent to treat these assessments with more caution and assess their confidence as **'Low'**.

The number of articles that reported the effects of metals on larvae and embryos alone is also dominated by studies on the effect of copper (Table 1.4). The evidence suggests that *Mytilus* larvae and embryos are highly sensitive to copper, lead, and zinc, plus molybdenum and manganese although the last two are based on single papers. There is also evidence that organotins result in 'severe' (>75%) mortality in larvae and embryos.

Across the entire contaminant group, there is evidence that several metals, one nanoparticulate metal, and some organometals have been reported to cause 'severe' (>75%) mortalities in adult and juvenile mussels. Hence, an overall assessment of **'High**' sensitivity to metal contamination may be given based on the '**worst-case' scenario**.

Table 1.3. Summary of count of ranked mortalities reported in evidence review on the effects of metals in *Mytilus* spp. and resultant proposed sensitivity assessments for **adults and juveniles only**. (NS= Not sensitive, N= None, L= Low, M= Medium, H =High)

		Mortality (worst case reported)							Assessment		
Group	**Contaminant**	**Severe**	**Significant**	**Some**	**None**	**Sublethal**	**NR**	**Total**	**Resistance**	**Resilience**	**Sensitivity**
Metals & compounds											
	Cadmium	**5**	4	2	5	4	1	21	**N**	**L**	**H**
	Copper	**14**	11	1	6	9		41	**N**	**L**	**H**
	Dysprosium				**1**			1	H	H	**NS**
	Gadolinium				**1**			1	H	H	**NS**
	Iron		**1**					1	L	M	M
	Lead		**3**		1		1	5	L	M	M
	Mercury	**1**	2	5	1	1		10	**N**	**L**	**H**
	Methylmercury		**1**		1			2	L	M	M
	Neodymium				1			1	L	M	M
	Nickel				**1**		1	2	H	H	**NS**
	Selenium				**1**	1		2	H	H	**NS**
	Silver	**1**	2	1	1	4		9	**N**	**L**	**H**
	Titanium				**2**			2	H	H	**NS**
	Zinc	**3**	4	1	1	3	1	13	**N**	**L**	**H**
Metals & compounds (total)		**24**	**28**	10	23	22	4	111	**N**	**L**	**H**
Nanoparticulate metals											
	Copper				**3**			3	H	H	**NS**
	Silver				**3**			3	H	H	**NS**
	Titanium				**1**			1	H	H	**NS**
	Zinc		**1**					1	L	M	M
	Titanium dioxide				**2**			2	H	H	**NS**
	Gold				**1**			1	H	H	**NS**
Nanoparticulate metals (total)			**1**		10			11	**L**	**M**	**M**[5]
Organotin											
	Dibutyltin					**1**		1	H	H	**NS**
	Tributyltin			**1**	1	2		4	M	M	M
	Tributyltin oxide	**1**				1		2	**N**	**L**	**H**
Organotin (total)		**1**		1	1	4		7	**N**	**L**	**H**[6]
OrganoZinc											
	Zinc pyrithione	**1**						1	**N**	**L**	**H**
Grand Total		**26**	**29**	**11**	**34**	**26**	**4**	**130**	**N**	**L**	**H**[7]

[5] Based on a single paper while the remaining articles reported no observed mortalities so that 'Not sensitive' may be the more appropriate assessment, based on existing evidence.

[6] Based on a single paper while the remaining articles reported some or no mortalities or only sublethal effects so that 'Medium' sensitivity may be the more appropriate assessment, based on existing evidence.

[7] Across the entire group there is evidence that metals, one nanoparticulates and some organometals have been reported to cause severe mortalities in adult and juvenile mussels.

Table 1.4. Summary of count of ranked mortalities reported in evidence review on the effects of metals in *Mytilus* spp. and resultant proposed sensitivity assessments for **embryos and larvae only**. (NS= Not sensitive, N= None, L= Low, M= Medium, H =High)

		Mortality (worst case reported)							Assessment	
Group	Contaminant	Severe	Significant	Some	None	Sublethal	NR	Total	Resistance	Resilience	Sensitivity
Metals & salts											
	Arsenic		**1**					1	L	M	M
	Barium		**1**					1	L	M	M
	Cadmium		**6**	2				8	**L**	**M**	**M**
	Copper	**4**	14	1	1			20	**N**	**L**	**H**
	Lead	**1**	3					4	**N**	**L**	**H**
	Manganese	**1**						1	**N**	**L**	**H**
	Mercury		**7**					7	L	M	M
	Molybdenum	**1**						1	**N**	**L**	**H**
	Nickel		**2**	1				3	L	M	M
	Selenium		**1**					1	L	M	M
	Silver		**2**	1				3	L	M	M
	Strontium				**1**			1	H	H	**NS**
	Zinc	**1**	4					5	**N**	**L**	**H**
	Chromium		**1**					1	L	M	M
Metals & salts (total)		**8**	**42**	5	2			**57**	**N**	**L**	**H**
Nanoparticulate metals											
	Iron		**2**					2	L	M	M
	Titanium		**1**					1	L	M	M
Nanoparticulate metals (total)			**3**					3	**L**	**M**	**M**
Organotin											
	Dibutyltin	**1**						1	**N**	**L**	**H**
	Tributyltin		**3**					3	L	M	M
	Tributyltin oxide	**3**						3	**N**	**L**	**H**
Organotin (total)		**4**	**3**					**7**	**N**	**L**	**H**
OrganoZinc											
	Zinc pyrithione		**1**					**1**	L	M	M
Grand Total		**12**	**49**	**5**	**2**			**68**	**N**	**L**	**H**

1.3 *Mytilus* spp. – Synthetics

A total of 70 articles were selected from 2494 articles. These 70 articles focused on the physiological effects of exposure to synthetic contaminants on *Mytilus* spp. The range of ranked mortalities reported in the 70 papers examined is shown in Figure 1.10.

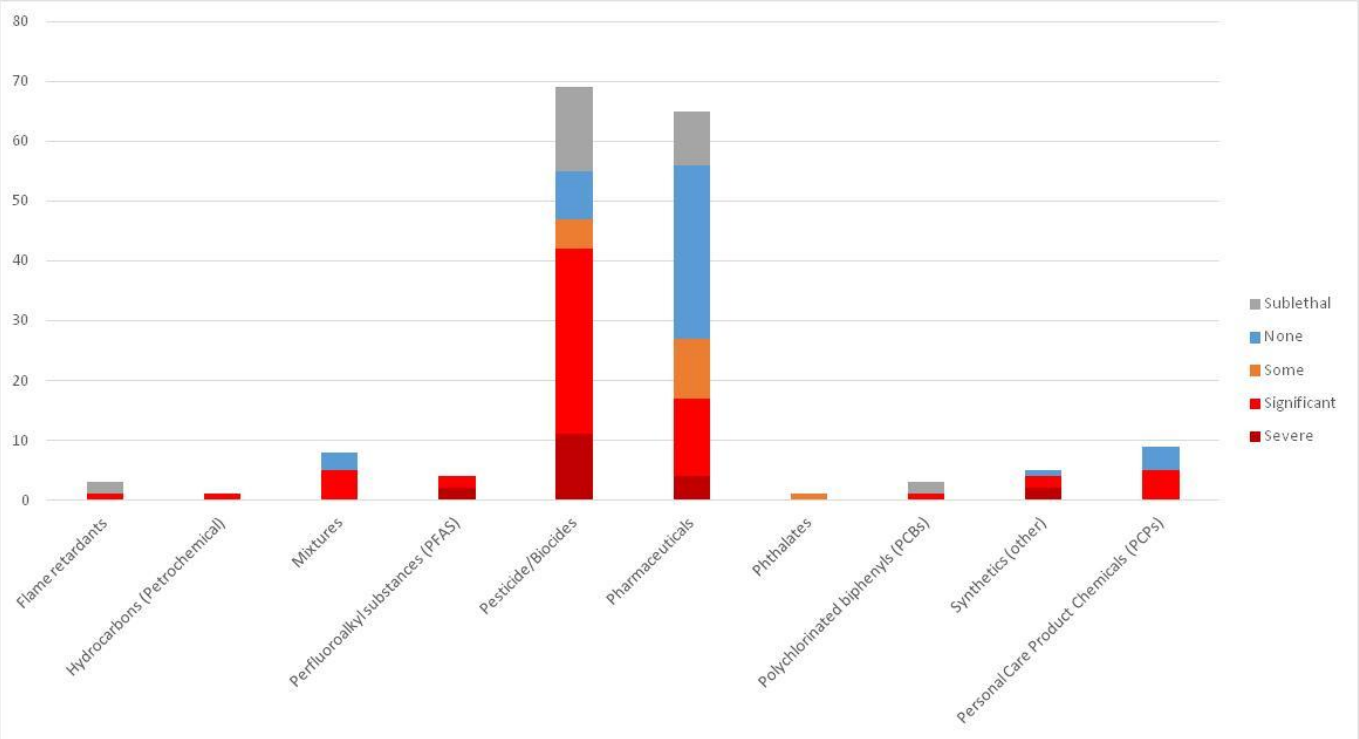

Figure 1.10. Count of ranked mortality due to exposure to synthetic contaminants in *Mytilus* spp.. Mortality is ranked as follows: 'Severe' (>75%), 'Significant' (25-75%), 'Some' (<25%), 'None' (no mortality reported), and 'Sublethal' effects. Note some articles are included more than once because they examined several different combinations of contaminant.

1.3.1 Flame retardants

Only two of the 70 articles selected examined the physiological effects of flame retardants on *Mytilus* spp.

- Barón *et al.* (2016) exposed *Mytilus galloprovincialis* adults to Decabromodiphenyl ether (56, 100, and 200 µg/l) and Dechlorane Plus (5.6, 56, and 100 µg/l) for a period of six days in semi-static exposure conditions. Exposure to either of the chemicals at the tested concentrations did not significantly affect clearance rates after six days of exposure.
- Fabbri *et al.* (2014) investigated the effects of eight contaminants on *Mytilus galloprovincialis* embryotoxicity during a 48-hour exposure experiment. The effects of different compounds representative of endocrine disrupting chemicals were tested in a wide concentration range (0.01,0.1,1,10,100,1000 µg/l). The flame retardant Tetrabromo bisphenol A showed a dose-dependent increase in the percentage of abnormal larvae in response to increasing concentration. Established NOEC, LOEC, and EC_{50} values were as follows 0.01 µg/l, 0.1 µg/l, and 5.52 µg/l.

1.3.2 Hydrocarbons

Fabbri *et al.* (2014) investigated the effects of eight contaminants on *Mytilus galloprovincialis* embryotoxicity during a 48-hour exposure experiment. The effects of different compounds representative of endocrine disrupting chemicals were tested in a wide concentration range (0.01, 0.1,

1, 10, 100, 1000 µg/l). The hydrocarbon Bisphenol A showed dose-dependent increase in the percentage of abnormal larvae in response to increasing concentration. The established NOEC, LOEC, and EC_{50} values were as follows 0.01 µg/l, 0.1 µg/l, and 3.68 µg/l.

1.3.3 Mixtures

Only one of the articles examined the physiological effects of contaminant mixtures on *Mytilus* spp.

Dispersants

Swedmark *et al.* (1973) investigated the effects of oil dispersants on the survival of *Mytilus edulis* after 96 hours of exposure and after 96 hours of exposure with 48 hours recovery in clean seawater. In addition, the effect of the dispersants on byssal activity and shell closure was investigated. Exposure to BP 1100X, Corexit 8666 or Fina-sol OSR2 did not cause any significant mortality during a four-day exposure period. However, exposure to Berol TL 188, BP1100, Fina-Sol SC and Nonylphenoxy polyethoxy ethanol caused significant mortality of *Mytilus edulis* during the four-day exposure period (Table 1.5).

Table 1.5. Range of 96-hour LC_{50}s, with and without 48 hours recovery in *Mytilus edulis* exposed to a range of dispersants (Swedmark *et al.*, 1973).

Dispersant	LC_{50} (96 hours) (mg/l)	LC_{50} (96-hour) after 48 hours recovery (mg/l)
BP 1100X:	>688	>688
Corexit 8666	>940	>940
Fina-sol OSR2	>700	>700
Berol TL 188	800	400
BP1100	>1000	250
Fina-Sol SC	>110	90
Nonylphenoxy polyethoxy ethanol	12	10
Polyclens TS 7	>984	>984
Berol TL 198	>1050	>1050
Corexit 7664	>1000	NR

1.3.4 Perfluoroalkyl substances (PFAS)

Only two of the selected articles examined the physiological effects of perfluoroalkyl substances (PFAS) on *Mytilus* spp.

- Hayman *et al.* (2021) investigated the toxicity of perfluorooctanoic sulphonate (PFOS) and perfluorooctanoic acid (PFOA) on larval development and survival. For PFOS the EC_{20} and EC_{50} that resulted in abnormal larvae development were 0.94 and 1.1 mg/l, respectively. Complete (100%) mortality occurred at >2mg/l PFOS, with LC_{20} and LC_{50} values determined at 0.93 and 1.07 mg/l, respectively. For PFOA the EC_{20} and EC_{50} that resulted in abnormal larvae development were 3.47 and 12 mg/l, respectively. Complete (100%) mortality occurred at 52 mg/l PFOA with LC_{20} and LC_{50} values determined to be 3.18 and 9.98 mg/l.
- Fabbri *et al.* (2014) investigated the effects of eight contaminants on *Mytilus galloprovincialis* embryotoxicity during a 48-hour exposure experiment. The effects of different compounds representative of endocrine disrupting chemicals were tested in a wide concentration range (0.01,0.1,1,10,100,1000 µg/L). The tested perfluoroalkyl substances showed a dose-dependent increase in the percentage of abnormal larvae in response to increasing concentration. For both perfluorooctanoic acid (PFOA) and perfluorooctanoic sulphonate (PFOS) the established NOEC and

LOEC values were 0.01 µg/l and 0.1 µg/l. The perfluoroalkyl substances PFOA and PFOS showed significant increase in abnormal larval development from 0.1 mg/l (17% and 27%, respectively). Maximal effects were observed at 100 mg/l (about 40% and 50%, respectively) with no further increase in percentage of abnormal development at higher concentrations.

1.3.5 Personal Care Product chemicals (PCPs)

Only four articles examined the effects of Personal Care Product (PCPs) on *Mytilus* spp..

- Gomez *et al.* (2012) investigated the bioconcentration of two pharmaceuticals (benzodiazepines: Diazepam and Tetrazepam) and two personal care products (UV filters: Octocrylene and 2-Ethyl-hexyl-4-methoxycinnamate) in *Mytilus galloprovincialis*. Significant mortality did not occur during the experiments and the condition index of the exposed mussels was not significantly different from the controls.
- Paredes *et al.* (2014) investigated the toxicity of four UV filters, 2-Ethyl-hexyl-4-methoxycinnamate (EHMC), 4-Methylbenzylidene-camphor (4-MBC), Benzophenone-3 (BP-3) and Benzophenone-4 (BP-4) on the development of *Mytilus galloprovincialis* larvae. The most toxic UV filter was 4-MBC (EC_{50} 587.17 µg/l), then, with similar toxicity, EHMC (EC_{50} 3118.19 µg/L) and then BP-3 (EC_{50} 3472.59 µg/l). BP-4 was not toxic at the tested concentrations, with an EC_{50} of >10,000 µg/l.
- Giraldo *et al.* (2017) investigated the effects of UV Filters Ethylhexyl Dimethyl p-Aminobenzoic Acid and Octocrylene on *Mytilus galloprovincialis* development. Both contaminants caused abnormal larvae. The established NOEC, LOEC, and EC_{50} of Ethylhexyl Dimethyl p-Aminobenzoic Acid were 25, 100, and 130 µg/l, respectively. The established NOEC, LOEC and EC_{50} of Octocrylene were 20, 40 and >650 µg/l, respectively.
- Bordalo *et al.* (2020) exposed *Mytilus galloprovincialis* to two UV filters (Benzophenone-3 and dimethyl sulfoxide) at concentrations between 0.01 to 1 µg/l. Neither contaminant caused mortalities during the 96-hour exposure trial.

1.3.6 Pesticide/Biocide

Twenty-seven of the selected articles examined the physiological effects of pesticides on *Mytilus* spp. Organohalogens (27%), carbamate (18%) and organophosphate (15%) were the most studied contaminants. A total of 15 (56%) of the 27 articles reported lethal effects (Figure 1.11). The evidence is *summarized* below for articles that reported 'end points'.

- Adema & Vink (1981) investigated the toxicity of Dieldrin, pentachlorophenol and 3,4-dichloroaniline on the survival of *Mytilus edulis*. The established LC_{50} values for Dieldrin at 14 and 30 days of exposure were >200 µg/l and 180 µg/l, respectively. The LC_{50} values for pentachlorophenol at 4, 7, and 14 days exposure were 18,000 µg/l, 950 µg/l and 750 µg/l, respectively. The LC_{50} values of 3,4-dichloroaniline at 4, 7, and 21 days exposure were 9,500, 8,000, and 6,500 µg/l respectively.
- Armstrong & Millemann (1974) investigated the effects of the insecticide Sevin and 1-naphthol on six different development stages of *Mytilus edulis*. All of the development stages were affected by the insecticide and 1-hour EC_{50} values were established from the numbers of normal and abnormal development. The most sensitive developmental stage was the stage following fertilization, at the time of appearance of the first polar body. Thereafter, sensitivity decreased as age increased. The EC_{50} values of 1-naphthol were only determined for the unfertilized egg and the first polar body with values of 24.5 and 5.2 mg/l, respectively. The EC_{50} values of Sevin on the larval developmental stages ranged from 5.3 to 24 mg/l, and the EC_{50} of Sevin on the unfertilized egg was 20.7 mg/l.

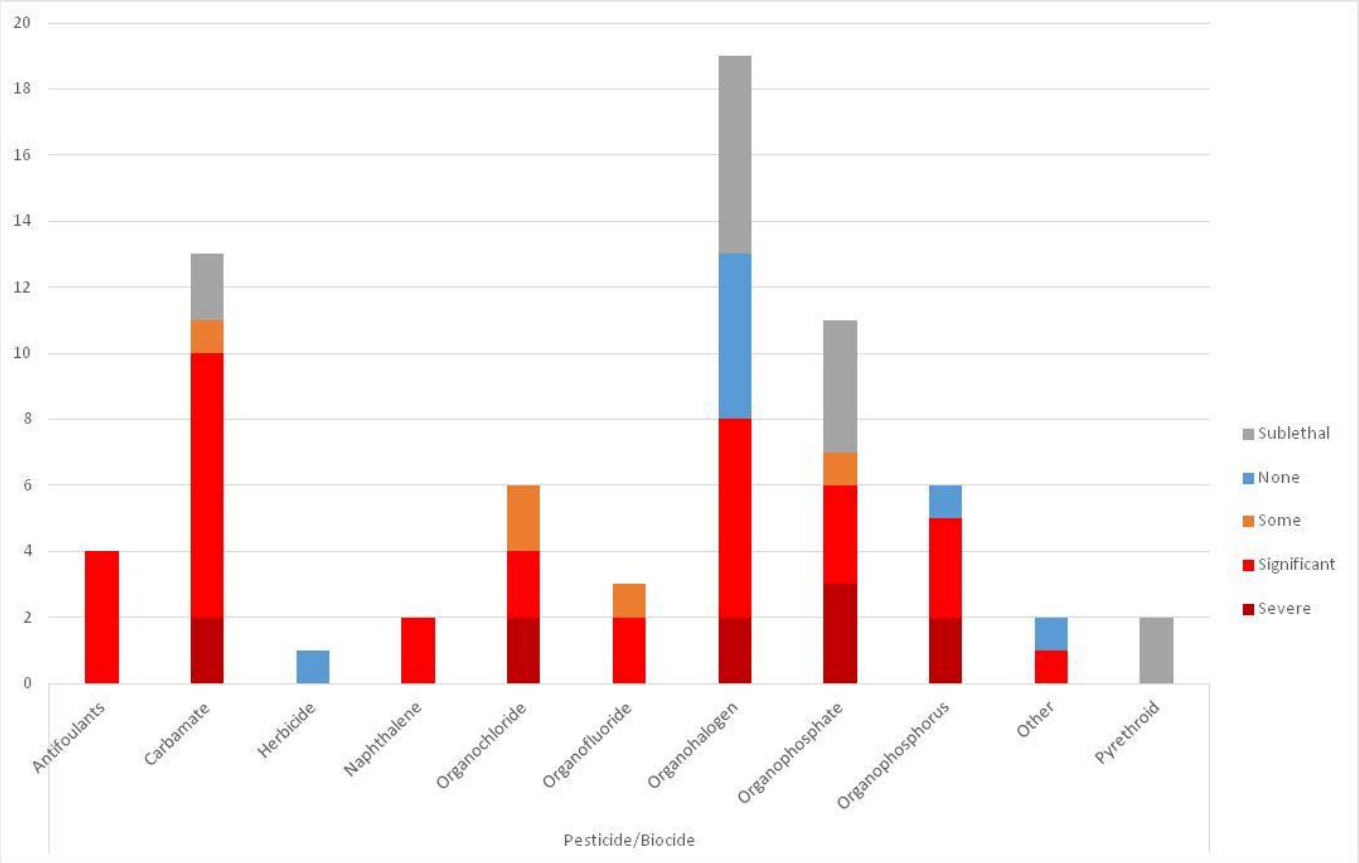

Figure 1.11. Count of ranked mortality due to exposure to pesticides or biocides in *Mytilus* spp.. Mortality is ranked as follows: 'Severe' (>75%), 'Significant' (25-75%), 'Some' (<25%), 'None' (no mortality reported), and 'Sublethal' effects. Note some articles are included more than once because they examined several different combinations of contaminant.

- Ayad *et al.* (2011) reported that concentrations of Cypermethrin up to 0.8 mg/l did not affect the time of survival in air of *Mytilus galloprovincialis* during 24 hours aerial exposure.
- Beiras & Bellas (2008) investigated the toxicity of the biocides Chlorpyrifos and Lindane on the inhibition of embryo development of *Mytilus galloprovincialis*, using the percentage of normal larvae as the end point. The EC_{10} and EC_{50} values were 79 and 154 µg/l for Chlorpyrifos, and 1,413 and 1,990 µg/l for Lindane.
- Bellas (2006) investigated the effects of antifouling biocides on the development of *Mytilus edulis*. Toxicity was quantified in terms of the EC_{50} (median effective concentration) and EC_{10} reducing embryogenesis success, larval growth, and larval settlement by 50% and 10% respectively. Chlorothalonil produced EC_{10} and EC_{50} values of 4.5 and 8.8 µg/l, whilst 'Sea- Nine 211' values were 7.1 and 11 µg/l. Dichlofluanid and Tolylfluanid showed similar toxicity, with EC_{10} values of 52 and 49 µg/l and EC_{50} values of 81 and 74 µg/l, respectively. Irgarol 1051 was the least toxic biocide with EC_{10} and EC_{50} of 797 and 1,540 µg/l. Sea-Nine 211 and Chlorothalonil were approximately 6–7 times more toxic than Dichlofluanid and Tolylfluanid, and 170 times more toxic than Irgarol 1051.
- Ernst & Doe (1989) compared the toxicity of the insecticide Fenitrothion flowable and Fenitrothion liquid technical formulations on the survival of *Mytilus edulis* during a 96-hour exposure, with an additional 96 hours in clean water to observe any delayed mortality. Significant mortalities occurred with LC_{50} values of 15 mg/l Fenitrothion flowable and 18.8 mg/l Fenitrothion liquid.
- Ernst *et al.* (1991) investigated the effects of Chlorothalonil (Bravo 500) toxicity on the survival of *Mytilus edulis* adults. They established a 96-hour LC_{50} value of 5.9 mg/l Chlorothalonil.

- Freitas *et al.* (2019b & 2019c) investigated the effects of Triclosan and Diclofenac on *Mytilus galloprovincialis* at different salinities during a 28-day exposure. No mortalities occurred throughout their experiments.
- Gowland *et al.* (2002) investigated the effects of Cypermethrin (Excis), at concentrations between 10 to 1,000 µg/l, on the aerial survival and shell closure of *Mytilus edulis*. Excis did not significantly affect the aerial survival of the exposed mussels compared to the controls. However, shell closure increased with increasing concentration of Excis.
- Karagiannis *et al.* (2011) investigated the effects of the herbicide Atrazine on the survival and byssus thread production of *Mytilus galloprovincialis*. The effects of Atrazine were monitored over 21 days at concentrations between 1 to 10 mg/l. Complete (100%) mortality occurred within five days at concentrations between 5 to 10 mg/l. In addition, byssal thread production was stopped. At the lower tested concentrations of 1 and 2 mg/l significant mortality occurred (32.5 and 60.83% respectively). The byssal thread production of the mussels in the 1 and 2 mg/l treatment was significantly reduced compared to the controls. After the 21-day exposure, the surviving mussels were then exposed to air and LT_{50} values were established. The control group had an LT_{50} of 5.14 days whilst the mussels that had been exposed to 1 and 2 mg/l Atrazine had LT_{50}s of 2.77 and 1.98 days, respectively.
- Lucu *et al.* (1980) investigated the toxicological effects of biocide Slimicide C-30 on the developmental stages of *Mytilus galloprovincialis*. The 96-hour EC_{50} was 0.07 mg/l.
- McHenery *et al.* (1997) investigated the effects of Dichlorvos exposure on *Mytilus edulis*. After 24 hours at concentrations of 3 mg/l and above, the mussels lost the ability to retract mantle fringes and close the valves of their shells, with an EC_{50} of 1.69 mg/l. Dichlorvos also affected the survival of *Mytilus edulis*, with a 24-hour LC_{50} of 8.2 mg/l.
- Pena-Llopis *et al.* (2002) investigated the toxicity of Fenitrothion and established 96-hour LC_{50} and LC_{85} of 8.4 and 12.1 mg/l respectively.
- Rao (1981) investigated the effects of two insecticides, gamma-hexachloran (Lindane) and Sevin (Carbaryl), on the survival of *Mytilus galloprovincialis* at 1, 2, 4, 6, 8, and 10 mg/l over seven days. The results indicated that the smaller mussels were more susceptible than larger mussels to both toxicants. At concentrations of 8 and 10 mg/l Lindane, total (100%) mortality occurred on day six for the small mussels and on day seven for the larger mussels. Sevin was less toxic as 10 mg/l caused 30% mortality of small mussels and 15% mortality of large mussels after seven days.
- Rao & Mane (1979) investigated the effects of Carbofos on the survival and respiration of *Mytilus galloprovincialis*. The survival of the mussels in the treatments between 2 and 12 mg/l decreased with increasing concentration of contaminant. All of the mussels in the 10 and 12 mg/l treatments were dead after seven days. But 100% survived at 0.5 and 1 mg/l Carbofos after the seven-day exposure. The oxygen consumption of the mussels varied depending on mussel size, exposure time and exposure concentration. At 1 mg/l, the small mussels initially expressed a rapid 19.4% increase in oxygen consumption compared to the control, followed by respiration suppression over the following four days, producing a 22.29% difference to the control. At 6 mg/l, the respiration of the small mussels was suppressed from the first day of exposure. At 1 mg/l, the large mussels had several peaks in respiration on the 1st, 3rd, 5th, and 6th day with increases in oxygen consumption of 88.60, 108.82, 34.71, and 11.56%, respectively. On the 2nd and 4th day, the respiration rate was less than the controls by 61.5 and 30.34%. The respiration of the large mussels initially decreased by 54.3% on the second day at 6 mg/l, followed by a threefold increase in respiration on the third day, that was then followed by reduced respiration with a difference of 69.9% of the control by the sixth day.

- Serrano *et al.* (1995) investigated the toxicity of five pesticides on the survival of *Mytilus galloprovincialis*. The mussels were exposed to the pesticides at concentrations of 1, 3.2, 5.6, 10, 32, and 56 mg/l. Methidathion, Chlorfenvinphos, and Chlorpyrifos caused significant mortality and inhibited byssal thread production. The LC_{50} values of Methidathion, Chlorfenvinphos, and Chlorpyrifos were calculated at 30.1, 26.3, and 22.5 mg/l, respectively. However, Dimethoate and Phosmet did not cause significant effects on mortality or byssal thread production.
- Liu & Lee (1975) investigated the toxicity of the insecticides Sevin, Methoxychlor, and Malathion, and the herbicides Treflan and 2,4-D on *Mytilus edulis*. The survival and byssus thread attachment were assessed in adult mussels, in addition to embryo shell development, larval growth, and metamorphosis. 96-hour LC_{50} values were calculated for each of the contaminants based on the survival of adults, and 48-hour EC_{50} values were calculated based on larval developmental abnormalities (Table 1.6).

Table 1.6. 96-hour EC_{50}s and LC_{50} determined for a range of pesticides in *Mytilus edulis*.

Pesticide	96-hour EC_{50} (mg/l)	96-hour LC_{50} (mg/l)
Sevin	1.5	22.7
Methoxychlor	>0.075	>0.092
Malathion	13.4	
Treflan	>0.12	>0.42
2,4-D	211.7	259

1.3.7 Pharmaceuticals

A total of 28 articles examined the effects of pharmaceuticals on *Mytilus* spp. Adrenergic agonists (21%) and Analgesics (NSAIDs) (24%) were the most studied, followed by beta-blockers (12%), chemotherapy agents (8%), antidepressants (8%) and antihyperlipidemic agents[8] (8%) (Figure 1.12). The majority (70%) of the articles reported lethal effects. The evidence is summarized below.

- Capolupo *et al.* (2018) investigated the impacts of three pharmaceuticals (Propranolol[9] (PROP), 17-α ethinylestradiol[10] (EE2), and Gemfibrozil[11] (GEM) on gamete fertilization and embryonic development in early life stages of *Mytilus galloprovincialis*. Concentrations comparable to or higher than environmental concentrations were used; PROP (0.5, 5, 50 µg/l), EE2 (0.005, 0.05, 0.5 µg/l), and GEM (0.050, 0.500, 5 µg/l). PROP did not affect gamete fertilization at the concentrations tested. However, inhibitory effects on fertilization of 24% and 17.6% were observed at environmental levels of EE2 (0.500 µg/l) and GEM (5 µg/l), and EC_{10} values of 0.142 and 2.4 µg/l, respectively, were determined. The 48-hour embryotoxicity exposure to all three pharmaceuticals caused the onset of morphologically abnormal larvae. The development of normal larvae was reduced by 18.5% in the 50 µg/L PROP treatment. Significant reductions of 19.9, 29.5, and 32.0% normal larvae development was observed at 0.005, 0.05, 0.5 µg/l EE2, with an EC_{10} of 0.0025 µg/l. The percentage of normally developed larvae was reduced by 23.3% at 0.5 µg/l GEM.
- Estevez-Calvar *et al.* (2017) investigated the effects of the antidepressant Sertraline on the development of *Mytilus galloprovincialis* embryos. The results showed that Sertraline significantly affected the development of mussel larvae with an EC_{50} of 206.80 µg/l.

[8] Antihyperlipidemic agents are pharmaceuticals designed to reduce the level of lipids or lipoproteins in the blood.
[9] A beta-blocker designed to reduce blood pressure
[10] A human hormone used in birth-control medication
[11] A antihyperlipidemic agent

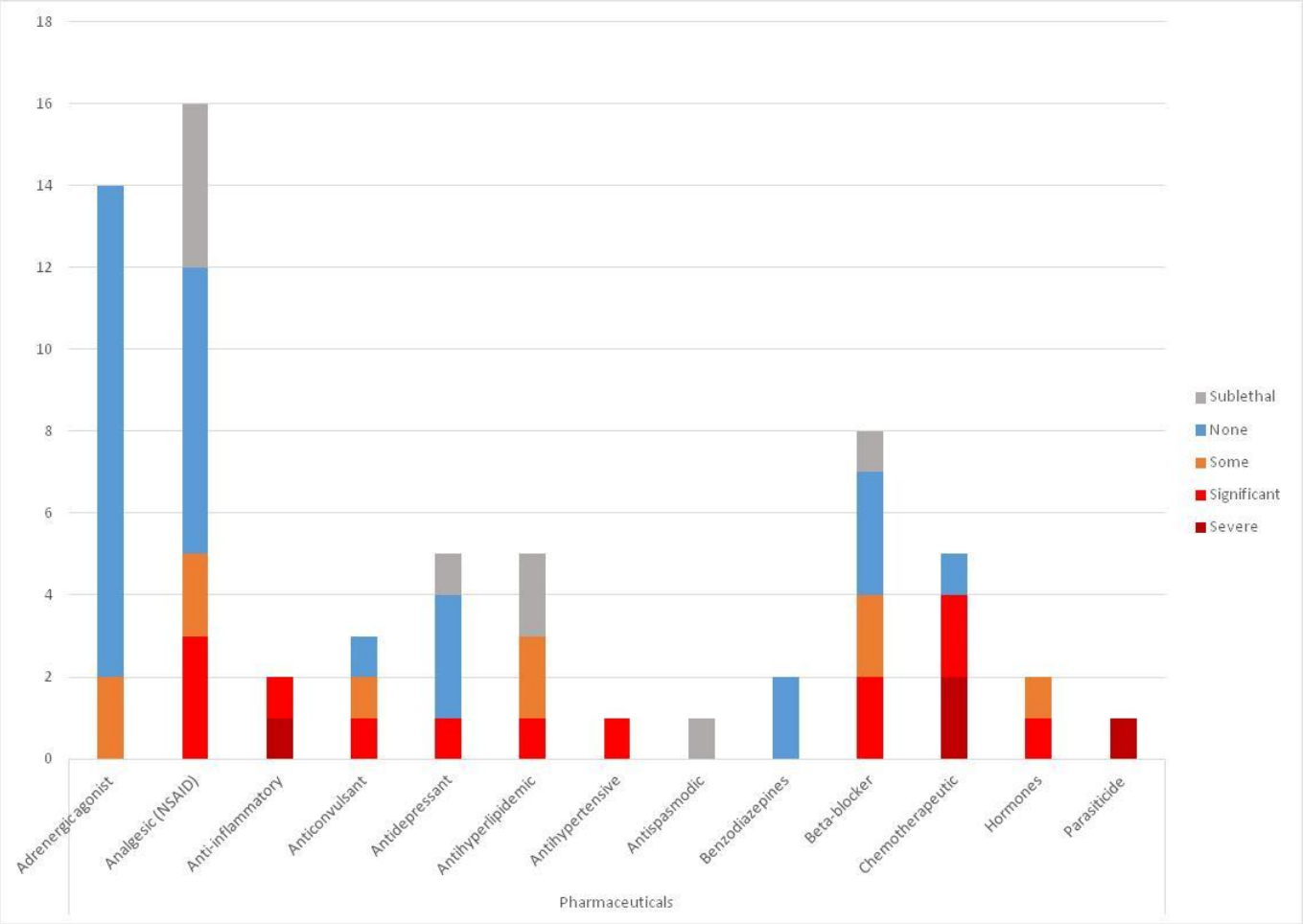

Figure 1.12. Count of ranked mortality due to exposure to pharmaceuticals in *Mytilus* spp.. Mortality is ranked as follows: 'Severe' (>75%), 'Significant' (25-75%), 'Some' (<25%), 'None' (no mortality reported), and 'Sublethal' effects. Note some articles are included more than once because they examined several different combinations of contaminant.

- Fabbri *et al.* (2014) investigated the effects of eight contaminants on *Mytilus galloprovincialis* embryos during a 48-hour exposure experiment. The effects of different compounds representative of endocrine disrupting chemicals were tested in a wide concentration range (0.01,0.1,1,10,100,1000 µg/l). The pharmaceuticals Ibuprofen[12] and Bezafibrate[13] showed dose-dependent increase in the percentage of abnormal larvae in response to increasing concentrations. The NOEC and LOEC values for Ibuprofen were calculated at 10 and 100 µg/l, respectively. The mussel embryos were more sensitive to Bezafibrate producing NOEC and LOEC values of 1 and 10 µg/l, respectively. Diclofenac[14] significantly affected mussel larval development at low concentrations 0.001 µg/l, but produced an inverted U-shaped dose response curve, with no effects at the highest tested concentration. The Diclofenac NOEC was calculated to be 0.001 µg/l.
- Franzellitti *et al.* (2019) investigated the toxicity of Carbamazepine[15] and Propranolol on the embryo/larvae stages of *Mytilus galloprovincialis* development. They tested a range of concentration between 0.01 and 1000 mg/l using a 48-hour embryotoxicity assay. The results showed both pharmaceuticals to significantly affected embryo development from environmentally realistic concentrations of the chemicals. The EC_{50}s of Carbamazepine and Propranolol were calculated at 0.82 and 1.34 µg/l respectively.

[12] Analgesic (NSAIDs)
[13] An antihyperlipidemic agent
[14] Analgesic (NSAIDs)
[15] An anticonvulsant used to treat epilepsy and neuropathic pain

- Politakis *et al.* (2018) exposed *Mytilus galloprovincialis* to 25 µg/l Buscopan[16] plus and Mesulid[17] for seven days before exposing the mussels to air, to determine the observed stress on stress response. Both Buscopan and Mesulid exposed mussels had significantly reduced LT_{50} values (3–4 days) compared to the controls (5-6 days).
- Yang *et al.* (2011) investigated the effects of neurotransmitter blockers (Amitriptyline, Atenolol, Butoxamine, Chlorpromazine, Idazoxan, and Rauwolscine) and Tetraethylammonium (TEA) on larval metamorphosis in *Mytilus galloprovincialis*. Mortality only occurred in the TAE and Rauwolscine treatments during the 96-hour study period, with low mortality of <5%. Larval metamorphosis was not inhibited by 10^{-3} M TEA or at any of the tested concentrations of Rauwolscine, Atenolol, and Butoxamine. However, Chlorpromazine and Amitriptyline inhibited larval metamorphosis. The metamorphosis of the larvae was inhibited by 50% at 1.6 x 10^{-6} M Chlorpromazine and 6.6 x 10^{-5} M Amitriptyline. Idazoxin also inhibited metamorphosis with an IC_{50} of 4.4 x 10^{-3} M.

1.3.8 Phthalates

Only one of the selected articles examined the physiological effects of phthalates on *Mytilus* spp. Sif *et al.* (2016) exposed *Mytilus galloprovincialis* to two treatment exposures of potassium hydrogen phthalate (KHP) at 250 mg and 500 mg/kg of mussel for the first treatment period for 21 days before exposing the same mussels to 750 mg and 1000 mg/kg for the second treatment period for 21 days. Mortality rates significantly increased from 0-7% to 10-21% during the second exposure period. Exposure to KHP had negative effects on the growth of the mussels with more significant effects for the larger mussels. Significant differences were also observed between the control and exposed mussels condition index.

1.3.9 Polychlorinated biphenyls (PCBs)

A total of three articles examined the effects of polychlorinated biphenyls on *Mytilus* spp.

- Eertman *et al.* (1993) investigated the effects of 1 µg/l PCBs (technical mixture Clophen A50, Bayer, Leverkusen) on the survival of *Mytilus edulis* in air. The survival time of PCB exposed mussels was significantly less than the controls. However, there was no difference in the survival time between mussels exposed to PCBs for three or four weeks.
- Eertman *et al.* (1996) exposed *Mytilus edulis* adults to 0.284 µg/l PCB 126 for a period of seven weeks before performing aerial exposure experiments to determine LT_{50} values for their survival in air. Mortalities were low (<5%) during the seven weeks exposure period. However, 50% mortality (LT_{50}) occurred within 5.2 days during the aerial exposure trial, which was significantly lower compared to the control.
- Roberts (1975) investigated the effects of PCBs (Aroclor 1254, Aroclor 1242) and pesticides (Carbaryl, Endosulfan, and Trichlorphon) on byssus formation and attachment in *Mytilus edulis*. The results showed several of the tested contaminants to cause reductions in byssal attachment.

1.3.10 Synthetics (other)

Organohalogens

- Cui *et al.* (2021) found that 10 µg/l of polyfluoroalkyl phosphate diester did not affect the growth or mortality of *Mytilus galloprovincialis* during a 72-hour exposure.

[16] An antispasmodic
[17] Analgesic (NSAIDs)

- Adema & Vink (1981) investigated the toxicity of 1,1,2-trichloroethane on the survival of *Mytilus edulis*. The established LC_{50} values for 1,1,2-trichloroethane at 4, 7 and 14 days of exposure were 110, 80, and 65 µg/l, respectively.

Fatty alcohol

Granmo & Jorgensen (1975) investigated the effects of long-term exposure to a non-ionic surfactant (Tallow alcohol decaethyleneglycolether) on the fertilization and development of *Mytilus edulis*. Spawning ability was not affected after five months exposure to 500, 100 and 1500 µg/l. However, fertilization was reduced compared to the control and larvae development was inhibited or delayed. Gametes from exposed parents were more sensitive to surfactant exposure than those from the control. Larvae from contaminant exposure parents had increased mortality compared to larvae from unexposed parents. Larvae from pre-exposed parents had 100% mortality at 1 mg/l surfactant, but at the same concentration larvae from unexposed parents had high survival and showed normal development.

Alcohol

Helmstetter *et al.* (1996) investigated the toxicity of 1 to 10% methanol on *Mytilus edulis.* The mortality and behaviour of the mussels was not affected at the lowest concentration of 7,950 mg/l (1% methanol). However, at concentrations of 15,900 mg/l and above the survival and behaviour of the mussels were significantly influenced. An LC_{50} of 15,900 mg/l, equivalent to 2% methanol was determined. At the two highest tested concentrations of 5 and 10% methanol (39,750 & 79,500 mg/l) 100% mortality occurred within 13.5 hours.

1.3.11 Surfactants

Hansen *et al.* (1997) investigated the physiological effects of the detergent linear alkylbenzene sulphonate (LAS) on blue mussel larvae in laboratory and mesocosm experiments. *Mytilus edulis* larvae were exposed to concentrations between 0 to 39 mg/l LAS. In the laboratory experiments, the larvae showed 50% mortality at 3.8 mg/L LAS after a 96-hour exposure. In addition, swimming speed and helix track diameter (swimming characteristics) were decreased with LAS exposure, with significant affects at 0.8 mg/l LAS. The grazing rate of the larvae was strongly influenced by LAS exposure, showing an EC_{50} of 1.4 mg/l. The growth rate of the larvae was significantly affected by LAS exposure and showed decreased growth in response to increased concentrations. A statistically significant reduction in growth was observed at 6.5 mg/l LAS. The growth rate of the larvae reduced to half at 0.82 mg/l LAS over nine days. During the mesocosm experiment, the larval population decreased in abundance within two days at concentrations as low as 0.08 mg LAS/L, because of significant mortality, but also due to settling. The settling success rate was reduced at the same LAS concentration 0.08mg/l as that at which mortality was observed to increase significantly. Also, the larvae showed delayed metamorphosis and reduced shell growth from LAS exposure.

Eisler *et al. (*1972) investigated the effects of sodium nitrilotriacetic acid (a chelating agent) on the survival of *Mytilus edulis.* They determined 24, 96, 168-hour LT_{50}s of >10,000, 6,100 and 3,400 mg/l respectively.

1.3.12 Pesticides, Pharmaceuticals, and Personal Care Products (PCPs)

Fabrello *et al.* (2021) investigated the toxicity of a mixture of glyphosate (an herbicide), 17a-ethinylestradiol (a synthetic estrogen), and amyl salicylate (a fragrance) on *Mytilus galloprovincialis*. Mussels were exposed for seven days to two realistic concentrations of the mixture (0.01 and 0.1 µg/l) before survival in air tests were performed. The results showed no significant differences in the survival time in air between the controls and the two tested concentrations.

1.3.13 Sensitivity assessment – Synthetic compounds

The number of articles that reported mortalities due to synthetic compounds in *Mytilus* spp. are summarized in Figure 1.10 and in Table 1.7 and Table 1.8 below. Relevant resistance ranks and resultant sensitivities are shown in Table 1.7 and Table 1.8 based on the weight of evidence and 'worst-case' approach outlined above.

In general, the evidence suggested that longer exposure times were required to understand the affects of exposure to synthetic contaminants on *Mytilus*, as mussels could close their shells for days. Hence, short term exposures (e.g. <48hrs) may underestimate sensitivity. This agrees with Widdows & Donkin (1992) who suggested that LC_{50} values in *Mytilus* gave a false impression of high tolerance because adult bivalves were able to close their valves and isolate themselves from extreme (potentially lethal) conditions for long periods (i.e. days).

The majority of articles reported a lethal response of exposure to synthetic compounds in *Mytilus* spp. A total of 57% of ranked mortalities reported in the evidence review were lethal ('Severe', 'Significant' or 'Some'), while 27% reported no mortality ('None') and 16% reported sublethal effects.

The majority of the articles examined pesticides/biocides and pharmaceuticals (Figure 1.10). A total of 15 (56%) of the 27 articles that examined pesticides reported lethal effects. The majority of the evidence suggested that pesticides resulted in lethal effects in adults and juvenile *Mytilus* spp. but that larval and embryos were probably more sensitive. Therefore, we can suggest that *Mytilus* spp. probably has a **'High'** sensitivity to pesticide exposure, with a few exceptions. The confidence is the assessment is probably **'Medium'** because of the number of articles examined and the consistency in the response.

However, 19 (70%) of the articles that examined pharmaceuticals reported lethal effects (Figure 1.12). The most lethal responses were shown by the larvae and embryos rather than adults and juveniles. Therefore, we can suggest that *Mytilus* spp. probably has a **'High'** sensitivity to the pharmaceutical examined especially in the larvae and developmental stages. The confidence is the assessment is probably **'Medium'** because of the number of articles examined and the consistency in the response.

The evidence on other synthetic contaminant types is more limited. The flame retardant Tetrabromo bisphenol A (TBBPA) caused mortality and abnormal development in larvae (Fabbri *et al.*, 2014) while another two flame retardants had no significant effects on adults (Barón *et al.*, 2016). Different types of surfactant caused lethal responses in larvae, embryos and in adults. PFAS exposure caused mortality in larvae and embryos but no studies on the effects on adult were found.

Nevertheless, the results shown in Table 1.7 and Table 1.8 suggest that *Mytilus* spp. is probably sensitive to a number of synthetic compounds, especially in early development or as larvae. Therefore, the sensitivity of *Mytilus* spp. to the 'Synthetic compounds' examined is assessed as **'High'** (resistance is **'None'** and resilience is **'Low'**) especially in larvae and developmental stages. Overall, the confidence in the assessment is probably **'Medium'** because of the number of articles examined and the consistency in the response.

Table 1.7. Summary of count of ranked mortalities reported in evidence review of the effects of synthetic compounds on *Mytilus* spp. and resultant proposed sensitivity assessments in **adults and juveniles only**. (N= None, L= low, M= Medium, H =High, NS= Not sensitive).

		Mortality (worst case reported)							Assessment		
Group	**Contaminant**	**Severe**	**Significant**	**Some**	**None**	**Sublethal**	**NR**	**Total**	**Resistance**	**Resilience**	**Sensitivity**
Flame retardants											
	Organohalogen					2		2	**H**	**H**	**NS**[18]
Mixtures											
	Dispersants		**4**		3			7	L	M	M
	Pesticide/Biocides, Pharmaceuticals, PPCPs						1	1	H	H	**NS**
Mixtures (total)			**4**		**3**		**1**	**8**	**L**	**M**	**M**
Personal Care Product Chemicals (PPCPs)											
	Ultraviolet (UV) filter				**4**			4	**H**	**H**	**NS**
Pesticide/Biocide											
	Carbamate	**1**	1			2		4	**N**	L	H
	Organochloride	**1**	1					2	**N**	L	H
	Organofluoride		**1**					1	L	M	M
	Organohalogen	**2**	4		4	6		15	**N**	L	H
	Organophosphate	**2**	2			4		8	**N**	L	H
	Organophosphorus	**2**	3		1		2	8	**N**	L	H
	Other				**1**			1	H	H	**NS**
	Pyrethroid					2		2	H	H	**NS**
Pesticide/Biocide (total)		**8**	**12**		**6**	**14**	**2**	**42**	**N**	**L**	**H**
Pharmaceuticals											
	Analgesic (NSAID)			**2**	7	4		13	M	M	M
	Anticonvulsant			**2**	1			3	M	M	M
	Antidepressant				2	1		3	H	H	**NS**
	Antihyperlipidemic					2		2	H	H	**NS**
	Antispasmodic					1	1	2	H	H	**NS**
	Benzodiazepines				2			2	H	H	**NS**
	Beta-blocker		**1**	1		1		3	L	M	M
	Chemotherapeutic		**1**		1			2	L	M	M
Pharmaceuticals (total)			**2**	**5**	**13**	**9**	**1**	**30**	**L**	**M**	**M**
Phthalates											
	Phthalates			1				1	M	M	M[19]
Polychlorinated biphenyls (PCBs)											
	PCBs		**1**			2	1	4	**L**	**M**	**M**
Synthetics (other)											
	Alcohol	**1**						1	**N**	L	H
	Surfactant	**1**						1	**N**	L	H
	Organohalogen		**1**		1			2	L	M	M
Synthetics (other) (total)		**2**	**1**		**1**			**4**	**N**	**L**	**H**
Grand Total		**10**	**20**	**6**	**27**	**27**	**5**	**95**	**N**	**L**	**H**

[18] Based on one article
[19] Based on one article

Table 1.8. Summary of count of ranked mortalities reported in evidence review of the effects of synthetic compounds on *Mytilus* spp. and resultant proposed sensitivity assessments **in embryos and larvae only**. (N= None, L= low, M= Medium, H =High, NS= Not sensitive).

		Mortality (worst case reported)							Assessment		
Group	**Contaminant**	**Severe**	**Significant**	**Some**	**None**	**Sublethal**	**NR**	**Total**	**Resistance**	**Resilience**	**Sensitivity**
Flame retardants											
	Organohalogen		**1**					1	**L**	**M**	**M**[20]
Hydrocarbons (Petrochemical)											
	Phenols		**1**					1	**L**	**M**	**M**
Perfluoroalkyl substances (PFAS)											
	Perfluorooctanesulfonic acid (PFOS)	**1**	1					2	**N**	L	H
	Perfluorooctanoic acid (PFOA)	**1**	1					2	**N**	L	H
Perfluoroalkyl substances (PFAS) (total)		**2**	**2**					**4**	**N**	**L**	**H**
Personal Care Product Chemicals (PPCPs)											
	Ultraviolet (UV) filter		**5**				1	6	L	M	M
Pesticide/Biocide											
	Antifoulants		**4**					4	L	M	M
	Carbamate	**1**	7	1				8	**N**	L	H
	Naphthalene		**1**					1	L	M	M
	Organochloride	**1**	1	2				4	**N**	L	H
	Organofluoride		**1**	1				2	L	M	M
	Organohalogen		**2**					2	L	M	M
	Organophosphate	**1**	1	1				3	**N**	L	H
	Other		**1**					1	L	M	M
Pesticide/Biocide (total)		**3**	**17**	**5**				**25**	**N**	**L**	**H**
Pharmaceutical											
	Adrenergic agonist			**2**	12			14	M	M	M
	Analgesic (NSAID)		**2**					2	L	M	M
	Anti-inflammatory	**1**	1					2	**N**	L	H
	Anticonvulsant		**1**					1	L	M	M
	Antidepressant		**1**		1			2	L	M	M
	Antihyperlipidemic		**1**	1				2	L	M	M
	Antihypertensive		**1**					1	L	M	M
	Beta-blocker		**1**	1	2			4	L	M	M
	Chemotherapeutic	**2**	1					3	**N**	L	H
	Hormones		**1**					1	L	M	M
	Parasiticide[21]	**1**						1	**N**	L	H
Pharmaceutical (Total)		**4**	**10**	**4**	**15**			**33**	**N**	**L**	**H**
Synthetics (other)											
	Surfactant		**1**					1	L	M	M
Grand Total		**9**	**37**	**9**	**15**		**1**	**71**	**N**	**L**	**H**

[20] Based on one article
[21] An anti-malarial drug

2 Bibliography.

Abel, P.D., 1976. Effect of some pollutants on the filtration rate of *Mytilus*. *Marine Pollution Bulletin*, **7** (12), 228-231. DOI https://doi.org/10.1016/0025-326X(76)90267-8

Adema, D.M.M. & Vink, I.G.J., 1981. A comparative study of the toxicity of 1,1,2-trichloroethane, dieldrin, pentachlorophenol and 3,4 dichloroaniline for marine and fresh water organisms. *Chemosphere*, **10** (6), 533-554. DOI https://doi.org/10.1016/0045-6535(81)90255-1

Ahsanullah, M., 1976. Acute toxicity of cadmium and zinc to seven invertebrate species from Western Port, Victoria. *Marine and Freshwater Research*, **27** (2), 187-196. DOI https://doi.org/10.1071/MF9760187

Akberali, H.B., Earnshaw, M.J. & Marriott, K.R.M., 1985. The action of heavy metals on the gametes of the marine mussel, *Mytilus edulis* (L.)-II. Uptake of copper and zinc and their effect on respiration in the sperm and unfertilized egg. *Marine Environmental Research*, **16** (1), 37-59. DOI https://doi.org/10.1016/0141-1136(85)90019-4

Alonso, A., Suarez, P., Ruiz, Y., Dobal, V. & San Juan, F., 2019. Gonadal Histopathological Disorders in *Mytilus galloprovincialis* Male Exposed to Tars Used in Mussel Farms. *Frontiers in Marine Science*, **6**. DOI https://doi.org/10.3389/fmars.2019.00577

Al-Subiai, S.N., Moody, A.J., Mustafa, S.A. & Jha, A.N., 2011. A multiple biomarker approach to investigate the effects of copper on the marine bivalve mollusc, *Mytilus edulis*. *Ecotoxicology and Environmental Safety*, **74** (7), 1913-1920. DOI https://doi.org/10.1016/j.ecoenv.2011.07.012

Amat, A., Pfohl-Leszkowicz, A., Burgeot, T. & Castegnaro, M., 2004. DNA adducts as a biomarker of pollution: Field study on the genotoxic impact evolution of the Erika oil spill on mussels (*Mytilus edulis*) over a period of eleven months. *Polycyclic Aromatic Compounds*, **24** (4-5), 713-732. DOI https://doi.org/10.1080/10406630490472338

Amiard-Triquet, C., Berthet, B., Metayer, C. & Amiard, J.C., 1986. Contribution to the ecotoxicological study of cadmium, copper and zinc in the mussel *Mytilus edulis*. *Marine Biology*, **92** (1), 7-13. DOI https://doi.org/10.1007/BF00392739

Annamaria, V.G., Chiara, L., Alessandra, A.N., Alvise, B., His, E. & Francesco, G.P., 2005. *Mytilus galloprovincialis* as bioindicator in embryotoxicity testing to evaluate sediment quality in the lagoon of Venice (Italy). *Chemistry and Ecology*, **21** (6), 455-463. DOI https://doi.org/10.1080/02757540500438516

Annicchiarico, C., Biandolino, F., Cardellicchio, N., Di Leo, A., Giandomenico, S. & Prato, E., 2007. Predicting toxicity in marine sediment in Taranto Gulf (Ionian Sea, Southern Italy) using Sediment Quality Guidelines and a battery bioassay. *Ecotoxicology*, **16** (2), 239-246. DOI https://doi.org/10.1007/s10646-006-0123-z

Armstrong, D.A. & Millemann, R.E., 1974. Effects of the insecticide sevin and its first hydrolytic product, 1-naphthol, on some early developmental stages of the bay mussel *Mytilus edulis*. *Marine Biology*, **28** (1), 11-15. DOI https://doi.org/10.1007/BF00389112

Avelelas, F., Martins, R., Oliveira, T., Maia, F., Malheiro, E., Soares, A., Loureiro, S. & Tedim, J., 2017. Efficacy and Ecotoxicity of Novel Anti-Fouling Nanomaterials in Target and Non-Target Marine Species. *Marine Biotechnology*, **19** (2), 164-174. DOI https://doi.org/10.1007/s10126-017-9740-1

Ayad, M.A., Fdil, M.A. & Mouabad, A., 2011. Effects of Cypermethrin (Pyrethroid Insecticide) on the Valve Activity Behavior, Byssal Thread Formation, and Survival in Air of the Marine Mussel *Mytilus*

galloprovincialis. *Archives of Environmental Contamination and Toxicology*, **60** (3), 462-470. DOI https://doi.org/10.1007/s00244-010-9549-7

Babcock, M. M., P. M. Harris, M. G. Carls, C. C. Brodersen, & S. D. Rice, 1998. Mussel bed restoration and monitoring, *Exxon Valdez Oil Spill Restoration Project Final Report* (Restoration Project 95090), National Oceanic and Atmospheric Administration, National Marine Fisheries Service, Auke Bay Laboratory, Juneau, Alaska.

Bakhmet, I.N., Kantserova, N.P., Lysenko, L.A. & Nemova, N.N., 2012. Effect of copper and cadmium ions on heart function and calpain activity in blue mussel *Mytilus edulis*. *Journal of Environmental Science and Health Part a-Toxic/Hazardous Substances & Environmental Engineering*, **47** (11), 1528-1535. DOI https://doi.org/10.1080/10934529.2012.680393

Balbi, T., Montagna, M., Fabbri, R., Carbone, C., Franzellitti, S., Fabbri, E. & Canesi, L., 2018. Diclofenac affects early embryo development in the marine bivalve *Mytilus galloprovincialis*. *Science of the Total Environment*, **642**, 601-609. DOI https://doi.org/10.1016/j.scitotenv.2018.06.125

Balbi, T., Smerilli, A., Fabbri, R., Ciacci, C., Montagna, M., Grasselli, E., Brunelli, A., Pojana, G., Marcomini, A., Gallo, G. & Canesi, L., 2014. Co-exposure to n-TiO2 and Cd2+ results in interactive effects on biomarker responses but not in increased toxicity in the marine bivalve *M. galloprovincialis*. *Science of the Total Environment*, **493**, 355-364. DOI https://doi.org/10.1016/j.scitotenv.2014.05.146

Baltas, H., Dalgic, G., Bayrak, E.Y., Sirin, M., Cevik, U. & Apaydin, G., 2016. Experimental study on copper uptake capacity in the Mediterranean mussel (*Mytilus galloprovincialis*). *Environmental Science and Pollution Research*, **23** (11), 10983-10989. DOI https://doi.org/10.1007/s11356-016-6306-0

Barón, E., Dissanayake, A., Vila, J., Crowther, C., Readman, J., Jha, A., Eljarrat, E. & Barcelo, D., 2016. Evaluation of the Genotoxic and Physiological Effects of Decabromodiphenyl Ether (BDE-209) and Dechlorane Plus (DP) Flame Retardants in Marine Mussels (*Mytilus galloprovincialis*). *Environmental Science & Technology*, **50**. DOI https://doi.org/10.1021/acs.est.5b05814

Baussant, T., Ortiz-Zarragoitia, M., Cajaraville, M.P., Bechmann, R.K., Taban, I.C. & Sanni, S., 2011. Effects of chronic exposure to dispersed oil on selected reproductive processes in adult blue mussels (*Mytilus edulis*) and the consequences for the early life stages of their larvae. *Marine Pollution Bulletin*, **62** (7), 1437-1445. DOI https://doi.org/10.1016/j.marpolbul.2011.04.029

Beaumont, A.R. & Budd, M.D., 1984. High mortality of the larvae of the common mussel at low concentrations of tributyltin. *Marine Pollution Bulletin*, **15** (11), 402-405. DOI https://doi.org/10.1016/0025-326X(84)90256-X

Beaumont, A.R. & Toro, J.E., 1996. Allozyme genetics of *Mytilus edulis* subjected to copper and nutritive stress. *Journal of the Marine Biological Association of the United Kingdom*, **76** (4), 1061-1071. DOI https://doi.org/10.1017/S0025315400040959

Beaumont, A.R., Tserpes, G. & Budd, M.D., 1987. Some effects of copper on the veliger larvae of the mussel *Mytilus edulis* and the Scallop *Pecten maximus* (Mollusca, Bivalvia). *Marine Environmental Research*, **21** (4), 299-309. DOI https://doi.org/10.1016/0141-1136(87)90052-3

Bebianno, M.J. & Langston, W.J., 1992. Cadmium induction of metallothionein synthesis in *Mytilus galloprovincialis*. *Comparative Biochemistry and Physiology Part C: Comparative Pharmacology*, **103** (1), 79-85. DOI https://doi.org/10.1016/0742-8413(92)90231-U

Bebianno, M.J. & Serafim, M.A., 1998. Comparison of metallothionein induction in response to cadmium in the gills of the bivalve molluscs *Mytilus galloprovincialis* and *Ruditapes decussatus*. *Science of the Total Environment*, **214** (1), 123-131. DOI https://doi.org/10.1016/S0048-9697(98)00059-X

Beiras, R. & Albentosa, M., 2004. Inhibition of embryo development of the commercial bivalves *Ruditapes decussatus* and *Mytilus galloprovincialis* by trace metals; implications for the

implementation of seawater quality criteria. *Aquaculture*, **230**, 205-213. DOI https://doi.org/10.1016/S0044-8486(03)00432-0

Beiras, R. & Bellas, J., 2008. Inhibition of embryo development of the *Mytilus galloprovincialis* marine mussel by organic pollutants; assessment of risk for its extensive culture in the Galician Rias. *Aquaculture*, **277** (3), 208-212. DOI https://doi.org/10.1016/j.aquaculture.2008.03.002

Beiras, R. & His, E., 1995. Effects of dissolved mercury on embryogenesis, survival and growth of *Mytilus galloprovincialis* mussel larvae. *Marine Ecology Progress Series*, **126** (1-3), 185-189. DOI https://doi.org/10.3354/meps126185

Bellas, J., 2006. Comparative toxicity of alternative antifouling biocides on embryos and larvae of marine invertebrates. *Science of the Total Environment*, **367** (2), 573-585. DOI https://doi.org/10.1016/j.scitotenv.2006.01.028

Bellas, J., Granmo, A. & Beiras, R., 2005. Embryotoxicity of the antifouling biocide zinc pyrithione to sea urchin (Paracentrotus lividus) and mussel (*Mytilus edulis*). *Marine Pollution Bulletin*, **50** (11), 1382-1385. DOI https://doi.org/10.1016/j.marpolbul.2005.06.010

Berthet, B., Amiard, J.C., Amiard-Triquet, C., Martoja, M. & Jeantet, A.Y., 1992. Bioaccumulation, toxicity and physico-chemical speciation of silver in bivalve molluscs: ecotoxicological and health consequences. *Science of the Total Environment*, **125**, 97-122. DOI https://doi.org/10.1016/0048-9697(92)90385-6

Blanco-Rayon, E., Ivanina, A.V., Sokolova, I.M., Marigomez, I. & Izagirre, U., 2020. Sex and sex-related differences in gamete development progression impinge on biomarker responsiveness in sentinel mussels. *Science of the Total Environment*, **740**. DOI https://doi.org/10.1016/j.scitotenv.2020.140178

Bokn, T.L., Moy, F.E. & Murray, S.N., 1993. Long-term Effects of the Water-accomodated Fraction (WAF) of Diesel Oil on Rocky Shore Populations Maintained in Experimental Mesocosms. *Botanica Marina*, **36** (4), 313-320. DOI https://doi.org/10.1515/botm.1993.36.4.313

Bordalo, D., Leite, C., Almeida, A., Soares, A., Pretti, C. & Freitas, R., 2020. Impacts of UV Filters in *Mytilus galloprovincialis*: Preliminary Data on the Acute Effects Induced by Environmentally Relevant Concentrations. *Sustainability*, **12** (17). DOI https://doi.org/10.3390/su12176852

Børseth, J.F., Aunaas, T., Denstad, J.-P., Nordtug, T., Olsen, A.J., Schmid, R., Skjærvø, G. & Zachariassen, K.E., 1995. Transmembrane sodium energy gradient and calcium content in the adductor muscle of *Mytilus edulis* L. in relation to the toxicity of oil and organic chemicals. *Aquatic Toxicology*, **31** (3), 263-276. DOI https://doi.org/10.1016/0166-445X(94)00072-X

Boukadida, K., Banni, M., Gourves, P.Y. & Cachot, J., 2016. High sensitivity of embryo-larval stage of the Mediterranean mussel, *Mytilus galloprovincialis* to metal pollution in combination with temperature increase. *Marine Environmental Research*, **122**, 59-66. DOI https://doi.org/10.1016/j.marenvres.2016.09.007

Boukadida, K., Cachot, J., Morin, B., Clerandeau, C. & Banni, M., 2019. Moderate temperature elevation increase susceptibility of early-life stage of the Mediterranean mussel, *Mytilus galloprovincialis* to metal-induced genotoxicity. *Science of the Total Environment*, **663**, 351-360. DOI 10.1016/j.scitotenv.2019.01.215

Brooks, S.J., Farmen, E., Heier, L.S., Blanco-Rayón, E. & Izagirre, U., 2015. Differences in copper bioaccumulation and biological responses in three Mytilus species. *Aquat Toxicol*, **160**, 1-12. DOI https://doi.org/10.1016/j.aquatox.2014.12.018

Burbidge, F.J., Macey, D.J., Webb, J. & Talbot, V., 1994. A comparison between particulate (elemental) zinc and soluble zinc ($ZnCl_2$) uptake and effects in the mussel, *Mytilus edulis*. *Archives of*

Environmental Contamination and Toxicology, **26** (4), 466-472. DOI https://doi.org/10.1007/bf00214148

Cajaraville, M.P., J.A. Marigomez, and E. Angulo, 1992. "Comparative Effects of the Water Accommodated Fraction of Three Oils on Mussels: I. Survival, Growth and Gonad Development.".

Calabrese, A., MacInnes, J.R., Nelson, D.A., Greig, R.A. & Yevich, P.P., 1984. Effects of long-term exposure to silver or copper on growth, bioaccumulation and histopathology in the blue mussel *Mytilus edulis*. *Marine Environmental Research*, **11** (4), 253-274. DOI https://doi.org/10.1016/0141-1136(84)90038-2

Calabrese, A., Thurberg, F.P. & Gould, E., 1977. Effects of cadmium, mercury and silver on marine animals. *Marine Fisheries Review*, **39** (4), 5-11.

Canesi, L., Fabbri, R., Gallo, G., Vallotto, D., Marcomini, A. & Pojana, G., 2010. Biomarkers in *Mytilus galloprovincialis* exposed to suspensions of selected nanoparticles (Nano carbon black, C60 fullerene, Nano-TiO2, Nano-SiO2). *Aquatic Toxicology*, **100** (2), 168-177. DOI https://doi.org/10.1016/j.aquatox.2010.04.009

Canesi, L., Frenzilli, G., Balbi, T., Bernardeschi, M., Ciacci, C., Corsolini, S., Della Torre, C., Fabbri, R., Faleri, C., Focardi, S., Guidi, P., Kočan, A., Marcomini, A., Mariottini, M., Nigro, M., Pozo-Gallardo, K., Rocco, L., Scarcelli, V., Smerilli, A. & Corsi, I., 2014. Interactive effects of n-TiO2 and 2,3,7,8-TCDD on the marine bivalve *Mytilus galloprovincialis*. *Aquatic Toxicology*, **153**, 53-65. DOI https://doi.org/10.1016/j.aquatox.2013.11.002

Canty, M.N., Hagger, J.A., Moore, R.T.B., Cooper, L. & Galloway, T.S., 2007. Sublethal impact of short term exposure to the organophosphate pesticide azamethiphos in the marine mollusc *Mytilus edulis*. *Marine Pollution Bulletin*, **54** (4), 396-402. DOI https://doi.org/10.1016/j.marpolbul.2006.11.013

Canty, M.N., Hutchinson, T.H., Brown, R.J., Jones, M.B. & Jha, A.N., 2009. Linking genotoxic responses with cytotoxic and behavioural or physiological consequences: Differential sensitivity of echinoderms (Asterias rubens) and marine molluscs (*Mytilus edulis*). *Aquatic Toxicology*, **94** (1), 68-76. DOI https://doi.org/10.1016/j.aquatox.2009.06.001

Capolupo, M., Diaz-Garduno, B. & Martin-Diaz, M.L., 2018. The impact of propranolol, 17-ethinylestradiol, and gemfibrozil on early life stages of marine organisms: effects and risk assessment. *Environmental Science and Pollution Research*, **25** (32), 32196-32209. DOI https://doi.org/10.1007/s11356-018-3185-6

Capolupo, M., Valbonesi, P., Kiwan, A., Buratti, S., Franzellitti, S. & Fabbri, E., 2016. Use of an integrated biomarker-based strategy to evaluate physiological stress responses induced by environmental concentrations of caffeine in the Mediterranean mussel *Mytilus galloprovincialis*. *Science of the Total Environment*, **563**, 538-548. DOI https://doi.org/10.1016/j.scitotenv.2016.04.125

Carls, M.G., Babcock, M.M., Harris, P.M., Irvine, G.V., Cusick, J.A. & Rice, S.D., 2001. Persistence of oiling in mussel beds after the *Exxon Valdez* oil spill. *Marine Environmental Research*, **51** (2), 167-190. DOI https://doi.org/10.1016/s0141-1136(00)00103-3

Chalkiadaki, O., Dassenakis, M. & Lydakis-Simantiris, N., 2014. Bioconcentration of Cd and Ni in various tissues of two marine bivalves living in different habitats and exposed to heavily polluted seawater. *Chemistry and Ecology*, **30** (8), 726-742. DOI https://doi.org/10.1080/02757540.2014.917172

Coles, J.A., Farley, S.R. & Pipe, R.K., 1995. Alteration of the immune response of the common marine mussel *Mytilus edulis* resulting from exposure to cadmium. *Diseases of Aquatic Organisms*, **22**, 59-65. DOI https://doi.org/10.3354/dao022059

Coppola, F., Almeida, A., Henriques, B., Soares, A., Figueira, E., Pereira, E. & Freitas, R., 2017. Biochemical impacts of Hg in *Mytilus galloprovincialis* under present and predicted warming

scenarios. *Science of the Total Environment*, **601**, 1129-1138. DOI https://doi.org/10.1016/j.scitotenv.2017.05.201

Coppola, F., Henriques, B., Soares, A., Figueira, E., Pereira, E. & Freitas, R., 2018. Influence of temperature rise on the recovery capacity of *Mytilus galloprovincialis* exposed to mercury pollution. *Ecological Indicators*, **93**, 1060-1069. DOI https://doi.org/10.1016/j.ecolind.2018.05.077

Cotter, A., Phillips, D. & Ahsanullah, M., 1982. The significance of temperature, salinity and zinc as lethal factors for the mussel *Mytilus edulis* in a polluted estuary. *Marine Biology*, **68**, 135-141. DOI https://doi.org/10.1007/BF00397600

Cotter, A., Phillips, D. & Ahsanullah, M., 1982. The significance of temperature, salinity and zinc as lethal factors for the mussel *Mytilus edulis* in a polluted estuary. *Marine Biology*, **68**, 135-141. DOI https://doi.org/10.1007/BF00397600

Counihan, K.L., 2018. The physiological effects of oil, dispersant and dispersed oil on the bay mussel, *Mytilus trossulus*, in Arctic/Subarctic conditions. *Aquatic Toxicology*, **199**, 220-231. DOI https://doi.org/10.1016/j.aquatox.2018.04.002

Craddock, D.R., 1977. Acute toxicity effects of petroleum on Arctic and Subarctic marine organisms. In Malins, D.C. (ed.) *Effects of petroleum on Arctic and Subarctic marine environments and organisms. Vol. 2. Biological effects*, New York: Academic Press Inc., pp. 1-93.

Crump, R.G., Morley, H.S. & Williams, A.D., 1999. West Angle Bay, a case study. Littoral monitoring of permanent quadrats before and after the "*Sea Empress*" oil spill. In Edwards, R. and Sime, H. (eds.). *The Sea Empress oil spill*: Chartered Institution of Water and Environmental Management, pp. 207-225.

Cui, W., Zhijun, T., Chen, J., Wu, H., Geng, Q., Guo, M. & Yuxiu, Z., 2021. Uptake, Tissue Distribution and Elimination of 8:2 Polyfluoroalkyl Phosphate Diesters in *Mytilus galloprovincialis*. *Environmental Toxicology and Chemistry*, **40** (7), 1990-2002. DOI https://doi.org/10.1002/etc.5060

Curtis, T., Williamson, R. & Depledge, M., 2000. Simultaneous, long-term monitoring of valve and cardiac activity in the blue mussel *Mytilus edulis* exposed to copper. *Marine Biology*, **136**, 837-846. DOI https://doi.org/10.1007/s002270000297

Danellakis, D., Ntaikou, I., Kornaros, M. & Dailianis, S., 2011. Olive oil mill wastewater toxicity in the marine environment: Alterations of stress indices in tissues of mussel *Mytilus galloprovincialis*. *Aquatic Toxicology*, **101** (2), 358-366. DOI https://doi.org/10.1016/j.aquatox.2010.11.015

Davenport, J. & Manley, A., 1978. The detection of heightened seawater copper concentrations by the mussel *Mytilus edulis*. *Journal of the Marine Biological Association of the United Kingdom*, **58** (4), 843-850. DOI https://doi.org/10.1017/S0025315400056800

DeForest, D.K. & Schlekat, C.E., 2013. Species sensitivity distribution evaluation for chronic nickel toxicity to marine organisms. *Integrated Environmental Assessment and Management*, **9** (4), 580-589. DOI https://doi.org/10.1002/ieam.1419

Dixon, D.R. & Prosser, H., 1986. An investigation of the genotoxic effects of an organotin antifouling compound (bis(Tributyltin) oxide) on the chromosomes of the edible mussel, *Mytilus edulis*. *Aquatic Toxicology*, **8** (3), 185-195. DOI https://doi.org/10.1016/0166-445x(86)90064-0

Domouhtsidou, G.P. & Dimitriadis, V.K., 2000. Ultrastructural Localization of Heavy Metals (Hg, Ag, Pb, and Cu) in Gills and Digestive Gland of Mussels, *Mytilus galloprovincialis* (L.). *Archives of Environmental Contamination and Toxicology*, **38** (4), 472-478. DOI https://doi.org/10.1007/s002449910062

Donaghy, L., Hong, H.K., Kim, M., Park, H.S. & Choi, K.S., 2016. Assessment of the fitness of the mussel *Mytilus galloprovincialis* two years after the Hebei Spirit oil spill. *Marine Pollution Bulletin*, **113** (1-2), 324-331. DOI https://doi.org/10.1016/j.marpolbul.2016.10.007

Donkin, P., Widdows, J., Evans, S.V., Staff, F.J. & Yan, T., 1997. Effect of neurotoxic pesticides on the feeding rate of marine mussels (*Mytilus edulis*). *Pesticide Science*, **49** (2), 196-209. DOI https://doi.org/10.1002/(SICI)1096-9063(199702)49:2%3C196::AID-PS495%3E3.0.CO;2-C

Donkin, P., Widdows, J., Evans, S.V., Worrall, C.M. & Carr, M., 1989. Quantitative structure-activity relationships for the effect of hydrophobic organic chemicals on rate of feeding by mussels (*Mytilus edulis*). *Aquatic Toxicology*, **14** (3), 277-293. DOI https://doi.org/10.1016/0166-445X(89)90021-0

Dorn, P., 1976. The feeding behavior of *Mytilus edulis* in the presence of methylmercury acetate. *Bulletin of Environmental Contamination and Toxicology*, **15** (6), 714-719. DOI 10.1007/BF01685622

D'Silva, C. & Kureishy, T.W., 1978. Experimental studies on the accumulation of copper and zinc in the green mussel. *Marine Pollution Bulletin*, **9** (7), 187-190. DOI https://doi.org/10.1016/0025-326X(78)90176-5

Earnshaw, M.J., Wilson, S., Akberali, H.B., Butler, R.D. & Marriott, K.R.M., 1986. The action of heavy metals on the gametes of the marine mussel, *Mytilus edulis* (L.)—III. The effect of applied copper and zinc on sperm motilityin relation to ultrastructural damage and intracellular metal localisation. *Marine Environmental Research*, **20** (4), 261-278. DOI https://doi.org/10.1016/0141-1136(86)90052-8

Eertman, R.H.M., Wagenvoort, A.J., Hummel, H. & Smaal, A.C., 1993. Survival in air of the blue mussel *Mytilus edulis* L. as a sensitive response to pollution-induced environmental-stress. *Journal of Experimental Marine Biology and Ecology*, **170** (2), 179-195. DOI https://doi.org/10.1016/0022-0981(93)90151-d

Eertman, R.H.M., Wagenvoort, A.J., Hummel, H. & Smaal, A.C., 1993. Survival in air of the blue mussel *Mytilus edulis* L. as a sensitive response to pollution-induced environmental-stress. *Journal of Experimental Marine Biology and Ecology*, **170** (2), 179-195. DOI https://doi.org/10.1016/0022-0981(93)90151-d

Eertman, R.H.M., Zurburg, W., Schipper, C.A., Sandee, B. & Smaal, A.C., 1996. Effects of PCB 126 and cadmium on the anaerobic metabolism of the mussel *Mytilus edulis* L. *Comparative Biochemistry and Physiology C-Pharmacology Toxicology & Endocrinology*, **113** (2), 267-272. DOI https://doi.org/10.1016/0742-8413(95)02096-9

Egidius, E. & Møster, B., 1987. Effect of Neguvon and Nuvan treatment on crabs (*Cancer pagurus, C. maenas*), lobster (*Homarus gammarus*) and blue mussel (*Mytilus edulis*). *Aquaculture*, **60** (2), 165-168. DOI https://doi.org/10.1016/0044-8486(87)90309-7

Eisler, R., 1971. Cadmium Poisoning in *Fundulus heteroclitus* (Pisces: Cyprinodontidae) and other Marine Organisms. *Journal of the Fisheries Research Board of Canada*, **28** (9), 1225-1234. DOI https://doi.org/10.1139/f71-188

Eisler, R., Gardner, G., Hennekey, R., LaRoche, G., Wash, D. & Yevich, P., 1972. Acute toxicology of sodium nitrilotriacetic acid (NTA) and NTA-containing detergents to marine organisms. *Water Research*, **6** (9), 1009-1027. DOI https://doi.org/10.1016/0043-1354(72)90054-1

El-Shenawy, N.S., R. Greenwood, and I.M. Abdel-Nabi, ZI, 2006. Effect of atrazine and lindane on the scope for growth of marine mussels *Mytilus edulis*. *Dong wu xue bao.[Acta Zoologica Sinica]*, **52** (4), 712-723.

Ericson, H., Thorsén, G. & Kumblad, L., 2010. Physiological effects of diclofenac, ibuprofen and propranolol on Baltic Sea blue mussels. *Aquatic Toxicology*, **99** (2), 223-231. DOI https://doi.org/10.1016/j.aquatox.2010.04.017

Ernst, W., Doe, K., Jonah, P., Young, J., Julien, G. & Hennigar, P., 1991. The toxicity of chlorothalonil to aquatic fauna and the impact of its operational use on a pond ecosystem. *Arch Environ Contam Toxicol*, **21** (1), 1-9. DOI https://doi.org/10.1007/bf01055550

Ernst, W.R. & Doe, K.G., 1989. A Comparison of the Aquatic Toxicity of Fenitrothion Flowable and Fenitrothion Liquid Technical Formulations. *Water Quality Research Journal*, **24** (4), 553-568. DOI https://doi.org/10.2166/wqrj.1989.034

Estevez-Calvar, N., Canesi, L., Montagna, M., Faimali, M., Piazza, V. & Garaventa, F., 2017. Adverse effects of the SSRI antidepressant sertraline on early life stages of marine invertebrates. *Marine Environmental Research*, **128**, 88-97. DOI https://doi.org/10.1016/j.marenvres.2016.05.021

Fabbri, R., Montagna, M., Balbi, T., Raffo, E., Palumbo, F. & Canesi, L., 2014. Adaptation of the bivalve embryotoxicity assay for the high throughput screening of emerging contaminants in *Mytilus galloprovincialis*. *Marine Environmental Research*, **99**, 1-8. DOI https://doi.org/10.1016/j.marenvres.2014.05.007

Fabrello, J., Masiero, L., Finos, L., Marin, M.G. & Matozzo, V., 2021. Effects of a mixture of glyphosate, 17 alpha-ethynylestradiol and amyl salicylate on cellular and biochemical parameters of the mussel *Mytilus galloprovincialis*. *Marine Environmental Research*, **165**. DOI https://doi.org/10.1016/j.marenvres.2020.105247

Fdil, M.A., Mouabad, A., Outzourhit, A., Benhra, A., Maarouf, A. & Pihan, J.C., 2006. Valve movement response of the mussel *Mytilus galloprovincialis* to metals (Cu, Hg, Cd and Zn) and phosphate industry effluents from Moroccan Atlantic coast. *Ecotoxicology*, **15** (5), 477-486. DOI https://doi.org/10.1007/s10646-006-0083-3

Fitzpatrick, J.L., Nadella, S., Bucking, C., Balshine, S. & Wood, C.M., 2008. The relative sensitivity of sperm, eggs and embryos to copper in the blue mussel (*Mytilus trossulus*). *Comp Biochem Physiol C Toxicol Pharmacol*, **147** (4), 441-449. DOI https://doi.org/10.1016/j.cbpc.2008.01.012

Franzellitti, S., Balbi, T., Montagna, M., Fabbri, R., Valbonesi, P., Fabbri, E. & Canesi, L., 2019. Phenotypical and molecular changes induced by carbamazepine and propranolol on larval stages of *Mytilus galloprovincialis*. *Chemosphere*, **234**, 962-970. DOI https://doi.org/10.1016/j.chemosphere.2019.06.045

Franzellitti, S., Buratti, S., Capolupo, M., Du, B.W., Haddad, S.P., Chambliss, C.K., Brooks, B.W. & Fabbri, E., 2014. An exploratory investigation of various modes of action and potential adverse outcomes of fluoxetine in marine mussels. *Aquatic Toxicology*, **151**, 14-26. DOI https://doi.org/10.1016/j.aquatox.2013.11.016

Freitas, R., Cardoso, C.E.D., Costa, S., Morais, T., Moleiro, P., Lima, A.F.D., Soares, M., Figueiredo, S., Agueda, T.L., Rocha, P., Amador, G., Soares, A. & Pereira, E., 2020a. New insights on the impacts of e-waste towards marine bivalves: The case of the rare earth element Dysprosium. *Environmental Pollution*, **260**. DOI https://doi.org/10.1016/j.envpol.2019.113859

Freitas, R., Coppola, F., Costa, S., Manzini, C., Intone, L., Meucci, V., Soares, A., Pretti, C. & Sole, M., 2019b. Does salinity modulates the response of *Mytilus galloprovincialis* exposed to triclosan and diclofenac? *Environmental Pollution*, **251**, 756-765. DOI https://doi.org/10.1016/j.envpol.2019.04.115

Freitas, R., Coppola, F., Costa, S., Pretti, C., Intorre, L., Meucci, V., Soares, A. & Sole, M., 2019c. The influence of temperature on the effects induced by Triclosan and Diclofenac in mussels. *Science of the Total Environment*, **663**, 992-999. DOI https://doi.org/10.1016/j.scitotenv.2019.01.189

Freitas, R., Coppola, F., Henriques, B., Wrona, F., Figueira, E., Pereira, E. & Soares, A., 2017. Does pre-exposure to warming conditions increase *Mytilus galloprovincialis* tolerance to Hg contamination?

Comparative Biochemistry and Physiology C-Toxicology & Pharmacology, **203**, 1-11. DOI https://doi.org/10.1016/j.cbpc.2017.09.010

Freitas, R., Costa, S., Cardoso, C.E.D., Morais, T., Moleiro, P., Matias, A.C., Pereira, A.F., Machado, J., Correia, B., Pinheiro, D., Rodrigues, A., Colonia, J., Soares, A. & Pereira, E., 2020b. Toxicological effects of the rare earth element neodymium in *Mytilus galloprovincialis*. *Chemosphere*, **244**. DOI https://doi.org/10.1016/j.chemosphere.2019.125457

Freitas, R., Leite, C., Pinto, J., Costa, M., Monteiro, R., Henriques, B., Di Martino, F., Coppola, F., Soares, A., Sole, M. & Pereira, E., 2019a. The influence of temperature and salinity on the impacts of lead in *Mytilus galloprovincialis*. *Chemosphere*, **235**, 403-412. DOI https://doi.org/10.1016/j.chemosphere.2019.05.221

Freitas, R., Silvestro, S., Coppola, F., Costa, S., Meucci, V., Battaglia, F., Intorre, L., Soares, A., Pretti, C. & Faggio, C., 2020. Toxic impacts induced by Sodium lauryl sulfate in *Mytilus galloprovincialis*. *Comparative Biochemistry and Physiology a-Molecular & Integrative Physiology*, **242**. DOI https://doi.org/10.1016/j.cbpa.2020.110656

Freitas, R., Silvestro, S., Coppola, F., Meucci, V., Battaglia, F., Intorre, L., Soares, A., Pretti, C. & Faggio, C., 2019d. Biochemical and physiological responses induced in *Mytilus galloprovincialis* after a chronic exposure to salicylic acid. *Aquatic Toxicology*, **214**. DOI https://doi.org/10.1016/j.aquatox.2019.105258

Galindo, E.A.G., Rodriguez, J.C.P. & Barbosa, A.M., 2014. Cadmium, Copper and Zinc in the mussel Mytilus californianus (Conrad 1837) from the west coast of Baja California. *Revista Internacional De Contaminacion Ambiental*, **30** (3), 285-295.

Garron, C., Gagne, F., Ernst, W., Julien, G., Bernier, M. & Caldwell, C., 2005. Mercury contamination of marine sediments and blue mussels (*Mytilus edulis*) in the vicinity of a mercury cell chlor-alkali plant in Dalhousie, New Brunswick, Canada. *Water Quality Research Journal of Canada*, **40** (1), 1-15.

Géret, F., Jouan, A., Turpin, V., Bebianno, M.J. & Cosson, R.P., 2002. Influence of metal exposure on metallothionein synthesis and lipid peroxidation in two bivalve mollusks: the oyster (Crassostrea gigas) and the mussel (*Mytilus edulis*). *Aquatic Living Resources*, **15** (1), 61-66. DOI https://doi.org/10.1016/S0990-7440(01)01147-0

Giannapas, M., Karnis, L. & Dailianis, S., 2012. Generation of free radicals in haemocytes of mussels after exposure to low molecular weight PAH components: Immune activation, oxidative and genotoxic effects. *Comparative Biochemistry and Physiology C-Toxicology & Pharmacology*, **155** (2), 182-189. DOI https://doi.org/10.1016/j.cbpc.2011.08.001

Giraldo, A., Montes, R., Rodil, R., Quintana, J.B., Vidal-Linan, L. & Beiras, R., 2017. Ecotoxicological Evaluation of the UV Filters Ethylhexyl Dimethyl p-Aminobenzoic Acid and Octocrylene Using Marine Organisms Isochrysis galbana, *Mytilus galloprovincialis* and Paracentrotus lividus. *Archives of Environmental Contamination and Toxicology*, **72** (4), 606-611. DOI https://doi.org/10.1007/s00244-017-0399-4

Gissi, F., Wang, Z., Batley, G.E., Leung, K.M.Y., Schlekat, C.E., Garman, E.R. & Stauber, J.L., 2020. Deriving a Chronic Guideline Value for Nickel in Tropical and Temperate Marine Waters. *Environmental Toxicology and Chemistry*, **39** (12), 2540-2551. DOI https://doi.org/10.1002/etc.4880

Gomes, T., Pereira, C.G., Cardoso, C. & Bebianno, M.J., 2013a. Differential protein expression in mussels *Mytilus galloprovincialis* exposed to nano and ionic Ag. *Aquatic Toxicology*, **136-137**, 79-90. DOI https://doi.org/10.1016/j.aquatox.2013.03.021

Gomes, T., Araújo, O., Pereira, R., Almeida, A.C., Cravo, A. & Bebianno, M.J., 2013b. Genotoxicity of copper oxide and silver nanoparticles in the mussel *Mytilus galloprovincialis*. *Marine Environmental Research*, **84**, 51-59. DOI https://doi.org/10.1016/j.marenvres.2012.11.009

Gomes, T., Chora, S., Pereira, C.G., Cardoso, C. & Bebianno, M.J., 2014a. Proteomic response of mussels *Mytilus galloprovincialis* exposed to CuO NPs and Cu^{2+}: an exploratory biomarker discovery. *Aquat Toxicol*, **155**, 327-336. DOI https://doi.org/10.1016/j.aquatox.2014.07.015

Gomes, T., Pereira, C.G., Cardoso, C., Sousa, V.S., Teixeira, M.R., Pinheiro, J.P. & Bebianno, M.J., 2014b. Effects of silver nanoparticles exposure in the mussel *Mytilus galloprovincialis*. *Marine Environmental Research*, **101**, 208-214. DOI https://doi.org/10.1016/j.marenvres.2014.07.004

Gomes, T., Pereira, C.G., Cardoso, C., Pinheiro, J.P., Cancio, I. & Bebianno, M.J., 2012. Accumulation and toxicity of copper oxide nanoparticles in the digestive gland of *Mytilus galloprovincialis*. *Aquatic Toxicology*, **118-119**, 72-79. DOI https://doi.org/10.1016/j.aquatox.2012.03.017

Gomes, T., Pinheiro, J.P., Cancio, I., Pereira, C.G., Cardoso, C. & Bebianno, M.J., 2011. Effects of Copper Nanoparticles Exposure in the Mussel *Mytilus galloprovincialis*. *Environmental Science & Technology*, **45** (21), 9356-9362. DOI https://doi.org/10.1021/es200955s

Gomez, E., Bachelot, M., Boillot, C., Munaron, D., Chiron, S., Casellas, C. & Fenet, H., 2012. Bioconcentration of two pharmaceuticals (benzodiazepines) and two personal care products (UV filters) in marine mussels (*Mytilus galloprovincialis*) under controlled laboratory conditions. *Environmental Science and Pollution Research*, **19** (7), 2561-2569. DOI https://doi.org/10.1007/s11356-012-0964-3

Gomiero, A., Volpato, E., Nasci, C., Perra, G., Viarengo, A., Dagnino, A., Spagnolo, A. & Fabi, G., 2015. Use of multiple cell and tissue-level biomarkers in mussels collected along two gas fields in the northern Adriatic Sea as a tool for long term environmental monitoring. *Marine Pollution Bulletin*, **93** (1-2), 228-244. DOI https://doi.org/10.1016/j.marpolbul.2014.12.034

Gonzalez-Rey, M. & Bebianno, M.J., 2011. Non-steroidal anti-inflammatory drug (NSAID) ibuprofen distresses antioxidant defense system in mussel *Mytilus galloprovincialis* gills. *Aquatic Toxicology*, **105** (3-4), 264-269. DOI https://doi.org/10.1016/j.aquatox.2011.06.015

Gonzalez-Rey, M. & Bebianno, M.J., 2013. Does selective serotonin reuptake inhibitor (SSRI) fluoxetine affects mussel *Mytilus galloprovincialis*? *Environ Pollut*, **173**, 200-209. DOI https://doi.org/10.1016/j.envpol.2012.10.018

Gonzalez-Rey, M. & Bebianno, M.J., 2014. Effects of non-steroidal anti-inflammatory drug (NSAID) diclofenac exposure in mussel *Mytilus galloprovincialis*. *Aquatic Toxicology*, **148**, 221-230. DOI https://doi.org/10.1016/j.aquatox.2014.01.011

Gowland, B., Webster, L., Fryer, R., Davies, I., Moffat, C. & Stagg, R., 2002. Uptake and effects of the cypermethrin-containing sea lice treatment Excis (R) in the marine mussel, *Mytilus edulis*. *Environmental Pollution*, **120** (3), 805-811. DOI https://doi.org/10.1016/s0269-7491(02)00176-8

Grace, A.L. & Gainey, L.F., 1987. The effects of copper on the heart-rate and filtration-rate of *Mytilus edulis*. *Marine Pollution Bulletin*, **18** (2), 87-91. DOI https://doi.org/10.1016/0025-326x(87)90574-1

Granby, K. & Spliid, N.H., 1995. Hydrocarbons and organochlorines in common mussels from the Kattegat and the belts and their relation to condition indexes. *Marine Pollution Bulletin*, **30** (1), 74-82. DOI https://doi.org/10.1016/0025-326x(94)00104-h

Granmo, Å. & Jørgensen, G., 1975. Effects of fertilization and development of the common mussel *Mytilus edulis* after long-term exposure to a nonionic surfactant. *Marine Biology*, **33** (1), 17-20. DOI https://doi.org/10.1007/BF00394996

Grout, J.A. & Levings, C.D., 2001. Effects of acid mine drainage from an abandoned copper mine, Britannia Mines, Howe Sound, British Columbia, Canada, on transplanted blue mussels (*Mytilus edulis*). *Marine Environmental Research*, **51** (3), 265-288. DOI https://doi.org/10.1016/s0141-1136(00)00104-5

Guolan, H. & Yong, W., 1995. Effects of tributyltin chloride on marine bivalve mussels. *Water Research*, **29** (8), 1877-1884. DOI https://doi.org/10.1016/0043-1354(94)00335-5

Hall, M.R., Moffett, J.W. & Gracey, A.Y., 2020. RNAseq Reveals Sensitive, Concentration-Dependent Transcriptional Markers of Copper in Mytilus californianus Larvae and Adults. *Frontiers in Marine Science*, **7**. DOI https://doi.org/10.3389/fmars.2020.572496

Hanna, S.K., Miller, R.J., Muller, E.B., Nisbet, R.M. & Lenihan, H.S., 2013. Impact of Engineered Zinc Oxide Nanoparticles on the Individual Performance of *Mytilus galloprovincialis*. *PLoS ONE*, **8** (4), e61800. DOI https://doi.org/10.1371/journal.pone.0061800

Hansen, B., Fotel, F.L., Jensen, N. & Wittrup, L., 1997. Physiological Effects of the Detergent Linear Alkylbenzene Sulphonate on Blue Mussel Larvae (*Mytilus edulis*) in Laboratory and Mesocosm Experiments. *Marine Biology*, **128** (4), 627-637. DOI https://doi.org/10.1007/s002270050129

Hawkins, A.J.S., Rusin, J., Bayne, B.L. & Day, A.J., 1989. The metabolic physiological-basis of genotype-dependent mortality during copper exposure in *Mytilus edulis*. *Marine Environmental Research*, **28** (1-4), 253-257. DOI https://doi.org/10.1016/0141-1136(89)90239-0

Hayman, N.T., Rosen, G., Colvin, M.A., Conder, J. & Arblaster, J.A., 2021. Aquatic toxicity evaluations of PFOS and PFOA for five standard marine endpoints. *Chemosphere*, **273**. DOI https://doi.org/10.1016/j.chemosphere.2021.129699

Helmstetter, A., Gamerdinger, A.P. & Pruell, R.J., 1996. Acute toxicity of methanol to *Mytilus edulis*. *Bulletin of Environmental Contamination and Toxicology*, **57** (4), 675-681. DOI https://doi.org/10.1007/s001289900243

Henriques, B., Coppola, F., Monteiro, R., Pinto, J., Viana, T., Pretti, C., Soares, A., Freitas, R. & Pereira, E., 2019. Toxicological assessment of anthropogenic Gadolinium in seawater: Biochemical effects in mussels *Mytilus galloprovincialis*. *Science of the Total Environment*, **664**, 626-634. DOI https://doi.org/10.1016/j.scitotenv.2019.01.341

Hietanen, B., Sunila, I. & Kristoffersson, R., 1988. Toxic effects of zinc on the common mussel *Mytilus edulis* L. (Bivalvia) in brackfish water. I. Physiological and histopathological studies. *Annales Zoologici Fennici*, **25**, 341-347.

Highsmith, R.C., Rucker, T.L., Stekoll, M.S., Saupe, S.M., Lindeberg, M.R., Jenne, R.N. & Erickson, W.P., 1996. Impact of the Exxon Valdez oil spill on intertidal biota. In Rice, S.D., Spies, R.B., Wolfe D.A., and Wright B.A. *Proceedings of the Exxon Valdez Oil Spill Symposium. American Fisheries Society Symposium, no. 18,*, American Fisheries Society, Anchorage, Alaska, USA, pp. 212-237.

His, E., Beiras, R. & Seaman, M.N.L., 2000. The assessment of marine pollution - Bioassays with bivalve embryos and larvae. In Southward, A.J., Tyler, P.A. and Young, C.M. (eds.). *Advances in Marine Biology, Vol 37*, pp. 1-178.

Hoare, K. & Davenport, J., 1994. Size-related variation in the sensitivity of the mussel, *Mytilus edulis*, to copper. *Journal of the Marine Biological Association of the United Kingdom*, **74** (4), 971-973. DOI https://doi.org/10.1017/S0025315400090214

Hoare, K., Davenport, J. & Beaumont, A., R., 1995. Effects of exposure and previous exposure to copper on growth of veliger larvae and survivorship of *Mytilus edulis* juveniles. *Marine Ecology Progress Series*, **120**, 163-168. DOI https://doi.org/doi:10.3354/meps120163

Hrs-Brenko, M., Claus, C. & Bubic, S., 1977. Synergistic effects of lead, salinity and temperature on embryonic-development of mussel *Mytilus galloprovincialis*. *Marine Biology*, **44** (2), 109-115. DOI https://doi.org/10.1007/bf00386951

Hu, W., Culloty, S., Darmody, G., Lynch, S., Davenport, J., Ramirez-Garcia, S., Dawson, K.A., Lynch, I., Blasco, J. & Sheehan, D., 2014. Toxicity of copper oxide nanoparticles in the blue mussel, *Mytilus edulis*: A redox proteomic investigation. *Chemosphere*, **108**, 289-299. DOI https://doi.org/10.1016/j.chemosphere.2014.01.054

Hvilsom, M.M., 1983. Copper-induced differential mortality in the mussel *Mytilus edulis*. *Marine Biology*, **76** (3), 291-295. DOI https://doi.org/10.1007/BF00393031

Ikavalko, J., Suni, S., Koskinen, K., Aalto, A., Jaanheimo, J. & Romantschuk, M., 2006. The use of cotton grass as oil sorbent in marine environmental protection - preliminary results from experiments. In Brebbia, C.A. and AntunesDoCarmo, J.S. (eds.). *Water Pollution Viii: Modelling, Monitoring and Management*, pp. 283-+. [WIT Transactions on Ecology and the Environment.

Jha, A.N., Hagger, J.A., Hill, S.J. & Depledge, M.H., 2000. Genotoxic, cytotoxic and developmental effects of tributyltin oxide (TBTO): an integrated approach to the evaluation of the relative sensitivities of two marine species. *Marine Environmental Research*, **50** (1-5), 565-573. DOI https://doi.org/10.1016/s0141-1136(00)00112-4

Jung, Y.H., Yoon, K.T., Shim, W.J. & Park, H.S., 2015. Short-Term Variation of the Macrobenthic Fauna Structure on Rocky Shores after the *Hebei Spirit* Oil Spill, West Coast of Korea. *Journal of Coastal Research*, **31** (1), 177-183. DOI https://doi.org/10.2112/jcoastres-d-13-00161.1

Kadar, E., Simmance, F., Martin, O., Voulvoulis, N., Widdicombe, S., Mitov, S., Lead, J.R. & Readman, J.W., 2010. The influence of engineered Fe2O3 nanoparticles and soluble ($FeCl_3$) iron on the developmental toxicity caused by CO_2-induced seawater acidification. *Environmental Pollution*, **158** (12), 3490-3497. DOI https://doi.org/10.1016/j.envpol.2010.03.025

Kadar, E., Simmance, F., Martin, O., Voulvoulis, N., Widdicombe, S., Mitov, S., Lead, J.R. & Readman, J.W., 2010. The influence of engineered Fe_2O_3 nanoparticles and soluble ($FeCl_3$) iron on the developmental toxicity caused by CO2-induced seawater acidification. *Environmental Pollution*, **158** (12), 3490-3497. DOI https://doi.org/10.1016/j.envpol.2010.03.025

Kadar, E., Tarran, G.A., Jha, A.N. & Al-Subiai, S.N., 2011. Stabilization of Engineered Zero-Valent Nanoiron with Na-Acrylic Copolymer Enhances Spermiotoxicity. *Environmental Science & Technology*, **45** (8), 3245-3251. DOI https://doi.org/10.1021/es1029848

Kaitala, S., 1988. Multiple Toxicity and Accumulation of Heavy Metals in Two Bivalve Mollusc Species. *Water Science and Technology*, **20** (6-7), 23-32. DOI https://doi.org/10.2166/wst.1988.0185

Karagiannis, D., Vatsos, I. & Angelidis, P., 2011. Effects of Atrazine on the Viability and the Formation of Byssus of the Mussel *Mytilus galloprovincialis*. *Aquaculture International*, **19**, 103-110. DOI https://doi.org/10.1007/s10499-010-9344-5

Labarta, U., Fernandez-Reiriz, M.J., Garrido, J.L., Babarro, J.M.F., Bayona, J.M. & Albaiges, J., 2005. Response of mussel recruits to pollution from the '*Prestige*' oil spill along the Galicia coast. A biochemical approach. *Marine Ecology Progress Series*, **302**, 135-145. DOI https://doi.org/10.3354/meps302135

Lapota, D., Rosenberger, D., Platter-Rieger, M. & Seligman, P., 1993. Growth and survival of *Mytilus edulis* larvae exposed to low levels of dibutyltin and tributyltin. *Marine Biology*, **115** (3), 413-419. DOI https://doi.org/10.1007/BF00349840

Lapota, D., Rosenberger, D., Platter-Rieger, M. & Seligman, P., 1993. Growth and survival of *Mytilus edulis* larvae exposed to low levels of dibutyltin and tributyltin. *Marine Biology*, **115** (3), 413-419. DOI https://doi.org/10.1007/BF00349840

Li, Y.F., Gu, Z.Q., Liu, H., Shen, H.D. & Yang, J.L., 2012. Biochemical response of the mussel Mytilus coruscus (Mytiloida: Mytilidae) exposed to in vivo sub-lethal copper concentrations. *Chinese Journal of Oceanology and Limnology*, **30** (5), 738-745. DOI https://doi.org/10.1007/s00343-012-1232-6

Libralato, G., Minetto, D., Totaro, S., Mičetić, I., Pigozzo, A., Sabbioni, E., Marcomini, A. & Volpi Ghirardini, A., 2013. Embryotoxicity of TiO2 nanoparticles to *Mytilus galloprovincialis* (Lmk). *Marine Environmental Research*, **92**, 71-78. DOI https://doi.org/10.1016/j.marenvres.2013.08.015

Liu, D.H.W. & Lee, J.M., 1975. Toxicity of Selected Pesticides to the Bay Mussel (*Mytilus edulis*). *Stanford Research Inst., Menlo Park, California; National Environmental Research Center, Corvallis, Oregon, EPA-660/3-75-016, U.S.EPA, Corvallis, OR:102 p.*, 110 pp. Available from https://nepis.epa.gov/Exe/ZyPURL.cgi?Dockey=9100LDU6.txt

Losso, C., His, E., Ghetti, P.F. & Volpi Ghirardini, A., 2004. Sensitivity of Embryotoxicity Test with *Mytilus galloprovincialis* (Lmk) Towards Some Compounds of Environmental Interest (Copper and Pesticides). *Environmental Technology*, **25** (7), 841-846. DOI https://doi.org/10.1080/09593330.2004.9619376

Lowe, D.M. & Pipe, R.K., 1987. Mortality and quantitative aspects of storage cell utilization in mussels, *Mytilus edulis*, following exposure to diesel oil hydrocarbons. *Marine Environmental Research*, **22** (4), 243-251. DOI https://doi.org/10.1016/0141-1136(87)90002-X

Lucu, C., Pavicic, J., Skreblin, M. & Mastrovic, M., 1980. Toxicological effects of biocide Slimicide C-30 on some marine invertebrates. *Mar. Pollut. Bull.;(United Kingdom)*, **11** (10), 294-296. DOI https://doi.org/10.1016/0025-326X(80)90167-8

Lussier, S.M., Boothman, W.S., Poucher, S., Champlin, D. & Helmstetten, A., 1999. Comparison of dissolved and total metals concentrations from acute tests with saltwater organisms. *Environmental Toxicology and Chemistry: An International Journal*, **18** (5), 889-898. DOI https://doi.org/10.1002/etc.5620180511

Lussier, S.M., Boothman, W.S., Poucher, S., Champlin, D. & Helmstetten, A., 1999. Comparison of dissolved and total metals concentrations from acute tests with saltwater organisms. *Environmental Toxicology and Chemistry: An International Journal*, **18** (5), 889-898. DOI https://doi.org/10.1002/etc.5620180511

Mamaca, E., Bechmann, R.K., Torgrimsen, S., Aas, E., Bjornstad, A., Baussant, T. & Le Floch, S., 2005. The neutral red lysosomal retention assay and Comet assay on haemolymph cells from mussels (*Mytilus edulis*) and fish (*Symphodus melops*) exposed to styrene. *Aquatic Toxicology*, **75** (3), 191-201. DOI https://doi.org/10.1016/j.aquatox.2005.08.001

Manley, A.R., 1983. The effects of copper on the behaviour, respiration, filtration and ventilation activity of *Mytilus edulis*. *Journal of the Marine Biological Association of the United Kingdom*, **63** (1), 205-222. DOI https://doi.org/10.1017/S0025315400049900

Manley, A.R., Gruffydd, L.D. & Almada-Villela, P.C., 1984. The effect of copper and zinc on the shell growth of *Mytilus edulis* measured by a laser diffraction technique. *Journal of the Marine Biological Association of the United Kingdom*, **64** (2), 417-427. DOI https://doi.org/10.1017/S0025315400030095

Martin, J.L.M., 1979. Schema of lethal action of copper on mussels. *Bulletin of Environmental Contamination and Toxicology*, **21** (1), 808-814. DOI https://doi.org/10.1007/BF01685509

Martin, J.L.M., 1979. Schema of lethal action of copper on mussels. *Bulletin of Environmental Contamination and Toxicology*, **21** (1), 808-814. DOI https://doi.org/10.1007/BF01685509

Martin, M., Osborn, K.E., Billig, P. & Glickstein, N., 1981. TOXICITIES OF 10 METALS TO CRASSOSTREA-GIGAS AND MYTILUS-EDULIS EMBRYOS AND CANCER-MAGISTER LARVAE. *Marine Pollution Bulletin*, **12** (9), 305-308. DOI https://doi.org/10.1016/0025-326x(81)90081-3

Martin, M., Osborn, K.E., Billig, P. & Glickstein, N., 1981. Toxicities of 10 metals to *Crassostrea gigas* and *Mytilus edulis* embryos and *Cancer magister* larvae. *Marine Pollution Bulletin*, **12** (9), 305-308. DOI 10.1016/0025-326x(81)90081-3

Martin-Diaz, L., Franzellitti, S., Buratti, S., Valbonesi, P., Capuzzo, A. & Fabbri, E., 2009. Effects of environmental concentrations of the antiepilectic drug carbamazepine on biomarkers and cAMP-mediated cell signaling in the mussel *Mytilus galloprovincialis*. *Aquatic Toxicology*, **94** (3), 177-185. DOI https://doi.org/10.1016/j.aquatox.2009.06.015

Mazzei, V., Longo, S., Conte, F., Pecoraro, R., Sal-Vaggio, A., Tibullo, D., Tiralongo, F., Lombardo, B.M. & Brundo, M.V., 2015. Effects of tributyltin and dibutyltin on sperm motility of *Mytilus galloprovincialis* (Mollusca: Mytilidae). *Thalassas*, **31** (2), 31-37.

McFadzen, I., Eufemia, N., Heath, C., Epel, D., Moore, M. & Lowe, D., 2000. Multidrug resistance in the embryos and larvae of the mussel *Mytilus edulis*. *Marine Environmental Research*, **50** (1-5), 319-323. DOI https://doi.org/10.1016/s0141-1136(00)00057-x

McHenery, J.G., LinleyAdams, G.E., Moore, D.C., Rodger, G.K. & Davies, I.M., 1997. Experimental and field studies of effects of dichlorvos exposure on acetylcholinesterase activity in the gills of the mussel, *Mytilus edulis* L. *Aquatic Toxicology*, **38** (1-3), 125-143. DOI https://doi.org/10.1016/s0166-445x(96)00834-x

Metayer, C., Amiard-Triquet, C. & Baud, J., 1990. Species-Related Variations of Silver Bioaccumulation and Toxicity to Three Marine Bivalves (Variations Inter-Specifiques de la Bioaccumulation et de la Toxicite de L'Argent a L'Egard de Trois Mollusques Bivalves Marins). *Water Resources Abstracts* **24** (8).

Mezzelani, M., Gorbi, S., Fattorini, D., d'Errico, G., Consolandi, G., Milan, M., Bargelloni, L. & Regoli, F., 2018. Long-term exposure of *Mytilus galloprovincialis* to diclofenac, Ibuprofen and Ketoprofen: Insights into bioavailability, biomarkers and transcriptomic changes. *Chemosphere*, **198**, 238-248. DOI https://doi.org/10.1016/j.chemosphere.2018.01.148

Micallef, S. & Tyler, P.A., 1987. Preliminary-observations of the interactions of mercury and selenium in *Mytilus edulis*. *Marine Pollution Bulletin*, **18** (4), 180-185. DOI https://doi.org/10.1016/0025-326x(87)90243-8

Micallef, S. & Tyler, P.A., 1990. Effect of mercury and selenium on the gill function of *Mytilus edulis*. *Marine Pollution Bulletin*, **21** (6), 288-292. DOI https://doi.org/10.1016/0025-326x(90)90592-v

Miramand, P. & Unsal, M., 1978. Acute Toxicity of Vanadium to some Marine Benthic and Phytoplanktonic Species. *Chemosphere*, **7** (10), 827-832.

Monteiro, R., Costa, S., Coppola, F., Freitas, R., Vale, C. & Pereira, E., 2019a. Evidences of metabolic alterations and cellular damage in mussels after short pulses of Ti contamination. *Science of the Total Environment*, **650**, 987-995. DOI https://doi.org/10.1016/j.scitotenv.2018.08.314

Monteiro, R., Costa, S., Coppola, F., Freitas, R., Vale, C. & Pereira, E., 2019b. Toxicity beyond accumulation of Titanium after exposure of *Mytilus galloprovincialis* to spiked seawater. *Environmental Pollution*, **244**, 845-854. DOI https://doi.org/10.1016/j.envpol.2018.10.035

Moore, J., 1997. Rocky shore transect monitoring in Milford Haven, October 1996. Imapcts of the *Sea Empress* oil spill. CCW Sea Empress Contract Report, Countryside Council for Wales, Bangor, Wales, 241, 90 pp.

Moore, M.N., Widdows, J., Cleary, J.J., Pipe, R.K., Salkeld, P.N., Donkin, P., Farrar, S.V., Evans, S.V. & Thomson, P.E., 1984. Responses of the mussel *Mytilus edulis* to copper and phenanthrene: Interactive effects. *Marine Environmental Research*, **14** (1), 167-183. DOI https://doi.org/10.1016/0141-1136(84)90077-1

Morgan, J.D., Mitchell, D.G. & Chapman, P.M., 1986. Individual and combined toxicity of manganese and molybdenum to mussel, *Mytilus edulis*, larvae. *Bulletin of Environmental Contamination and Toxicology*, **37** (1), 303-307. DOI https://doi.org/10.1007/BF01607765

Morrell, S.L., 1998. *Sea Empress* rocky shore impact assessment/monitoring: Dale fort Field Centre permanaent transects and rock pool studies. *CCW Sea Empress Contract Report*, *Countryside Council for Wales, Bangor, Wales, 319*, 14 pp.

Motta, C.M., Tizzano, M., Tagliafierro, A.M., Simoniello, P., Panzuto, R., Esposito, L., Migliaccio, V., Rosati, L. & Avallone, B., 2018. Biocide triclosan impairs byssus formation in marine mussels *Mytilus galloprovincialis*. *Environmental Pollution*, **241**, 388-396. DOI https://doi.org/10.1016/j.envpol.2018.05.064

Mudge, S.M., Salgado, M.A. & East, J., 1993. Preliminary investigations into sunflower oil contamination following the wreck of the M.V. Kimya. *Marine Pollution Bulletin*, **26** (1), 40-44. DOI https://doi.org/10.1016/0025-326X(93)90596-C

Myint, U.M. & Tyler, P.A., 1982. Effects of temperature, nutritive and metal stressors on the reproductive biology of *Mytilus edulis*. *Marine Biology*, **67** (2), 209-223. DOI https://doi.org/10.1007/BF00401287

Nadella, S.R., Fitzpatrick, J.L., Franklin, N., Bucking, C., Smith, S. & Wood, C.M., 2009. Toxicity of dissolved Cu, Zn, Ni and Cd to developing embryos of the blue mussel (Mytilus trossolus) and the protective effect of dissolved organic carbon. *Comparative Biochemistry and Physiology C-Toxicology & Pharmacology*, **149** (3), 340-348. DOI https://doi.org/10.1016/j.cbpc.2008.09.001

Nair, A., Ansari, Z., Harkantra, S. & Parulekar, A., 1977. Uptake of copper by the mussel *Mytilus viridis* L. *Indian Journal of Marine Sciences*, **6**, 90-91.

Nelson, D.A., Miller, J.E. & Calabrese, A., 1988. Effect of heavy metals on bay scallops, surf clams, and blue mussels in acute and long-term exposures. *Archives of Environmental Contamination and Toxicology*, **17** (5), 595-600. DOI https://doi.org/10.1007/BF01055828

Newey, S. & Seed, R., 1995. The effects of the Braer oil spill on rocky intertidal communities in south Shetland, Scotland. *Marine Pollution Bulletin*, **30** (4), 274-280. DOI https://doi.org/10.1016/0025-326X(94)00217-W

Oliveira, P., Almeida, A., Calisto, V., Esteves, V.I., Schneider, R.J., Wrona, F.J., Soares, A., Figueira, E. & Freitas, R., 2017. Physiological and biochemical alterations induced in the mussel *Mytilus galloprovincialis* after short and long-term exposure to carbamazepine. *Water Research*, **117**, 102-114. DOI https://doi.org/10.1016/j.watres.2017.03.052

Oskarsson, H., Wiklund, A.K.E., Thorsen, G., Danielsson, G. & Kumblad, L., 2014. Community Interactions Modify the Effects of Pharmaceutical Exposure: A Microcosm Study on Responses to Propranolol in Baltic Sea Coastal Organisms. *PLoS ONE*, **9** (4). DOI https://doi.org/10.1371/journal.pone.0093774

Pagano, G., His, E., Beiras, R., DeBiase, A., Korkina, L.G., Iaccarino, M., Oral, R., Quiniou, F., Warnau, M. & Trieff, N.M., 1996. Cytogenetic, developmental, and biochemical effects of aluminum, iron, and their mixture in sea urchins and mussels. *Archives of Environmental Contamination and Toxicology*, **31** (4), 466-474. DOI https://doi.org/10.1007/bf00212429

Paredes, E., Perez Fernández, S., Rodil, R., Quintana, J.B. & Beiras, R., 2014. Ecotoxicological evaluation of four UV filters using marine organisms from different trophic levels Isochrysis galbana, *Mytilus*

galloprovincialis, Paracentrotus lividus, and Siriella armata. *Chemosphere*, **104**. DOI https://doi.org/10.1016/j.chemosphere.2013.10.053

Pavicic, J., Skreblin, M., Kregar, I., Tusekznidaric, M. & Stegnar, P., 1994a. Embryo-larval tolerance of *Mytilus galloprovincialis*, exposed to the elevated sea-water metal concentrations .1. Toxic effects of Cd, Zn and Hg in relation to the metallothionein level. *Comparative Biochemistry and Physiology C-Pharmacology Toxicology & Endocrinology*, **107** (2), 249-257. DOI https://doi.org/10.1016/1367-8280(94)90048-5

Pavicic, J., Smodis, B., Skreblin, M., Kregar, I. & Stegnar, P., 1994b. Embryo larval tolerance of *Mytilus galloprovincialis*, exposed to elevated seawater metal concentrations .2. Stage-specific fluctuations in sensitivity toward Zn and Cd and their bioaccumulation into veliger larvae. *Comparative Biochemistry and Physiology C-Pharmacology Toxicology & Endocrinology*, **109** (1), 37-46. DOI https://doi.org/10.1016/1367-8280(94)00042-5

Pelletier, E., 1988. Acute toxicity of some methylmercury complexes to *Mytilus edulis* and lack of selenium protection. *Marine Pollution Bulletin*, **19** (5), 213-219. DOI https://doi.org/10.1016/0025-326x(88)90233-0

Pena-Llopis, S., Ferrando, M.D. & Pena, J.B., 2002. Impaired glutathione redox status is associated with decreased survival in two organophosphate-poisoned marine bivalves. *Chemosphere*, **47** (5), 485-497. DOI https://doi.org/10.1016/s0045-6535(01)00323-x

Pérez, M., García, M., Ruiz, D., Autino, J.C., Romanelli, G. & Blustein, G., 2016. Antifouling activity of green-synthesized 7-hydroxy-4-methylcoumarin. *Marine Environmental Research*, **113**, 134-140. DOI https://doi.org/10.1016/j.marenvres.2015.11.010

Peteiro, L.G., Babarro, J.M.F., Labarta, U. & Fernandez-Reiriz, M.J., 2006. Growth of *Mytilus galloprovincialis* after the Prestige oil spill. *Ices Journal of Marine Science*, **63** (6), 1005-1013. DOI https://doi.org/10.1016/j.icesjms.2006.03.010

Peteiro, L.G., Babarro, J.M.F., Labarta, U. & Fernandez-Reiriz, M.J., 2006. Growth of *Mytilus galloprovincialis* after the Prestige oil spill. *ICES Journal of Marine Science*, **63** (6), 1005-1013. DOI https://doi.org/10.1016/j.icesjms.2006.03.010

Peteiro, L.G., Filgueira, R., Labarta, U. & Fernandez-Reiriz, M.J., 2008. Growth and biochemical responses of the offspring of mussels directly affected by the "Prestige" oil spill. *ICES Journal of Marine Science*, **65** (4), 509-513. DOI https://doi.org/10.1093/icesjms/fsn014

Peters, J.R. & Granek, E.F., 2016. Long-term exposure to fluoxetine reduces growth and reproductive potential in the dominant rocky intertidal mussel, Mytilus californianus. *Science of the Total Environment*, **545**, 621-628. DOI https://doi.org/10.1016/j.scitotenv.2015.12.118

Politakis, N., Belavgeni, A., Efthimiou, I., Charalampous, N., Kourkouta, C. & Dailianis, S., 2018. The impact of expired commercial drugs on non-target marine species: A case study with the use of a battery of biomarkers in hemocytes of mussels. *Ecotoxicology and Environmental Safety*, **148**, 160-168. DOI https://doi.org/10.1016/j.ecoenv.2017.10.021

Poulsen, E., Riisgard, H.U. & Mohlenberg, F., 1982. ACCUMULATION OF CADMIUM AND BIOENERGETICS IN THE MUSSEL MYTILUS-EDULIS. *Marine Biology*, **68** (1), 25-29. DOI https://doi.org/10.1007/bf00393137

Prato, E. & Biandolino, F., 2007. Combined toxicity of mercury, copper and cadmium on embryogenesis and early stages of the *Mytilus galloprovincialis*. *Environmental Technology*, **28** (8), 915-920. DOI https://doi.org/10.1080/09593332808618851

Randall, N.P., Donnison, L.M., Lewis, P.J. & James, K.L., 2015. How effective are on-farm mitigation measures for delivering an improved water environment? A systematic map. *Environmental Evidence*, **4** (1), 18. DOI https://doi.org/10.1186/s13750-015-0044-5

Rao, M.B., 1981. Effect of gamma-Hexachloran and Sevin on the Survival of the Black Sea Mussel, *Mytilus galloprovincialis* Lam. *Hydrobiologia*, **78** (1), 33-37. DOI https://doi.org/10.1007/BF00011937

Rao, M.B., & U.K. Mane, 1978. The Effect of Carbofos on the Survival Rate and Respiration of Black Sea Mussels (*Mytilus galloprovincialis*). *Hydrobiological Journal*, **14** (6), 90-94.

Redpath, K.J., 1985. Growth Inhibition and Recovery in Mussels (*Mytilus edulis*) Exposed to Low Copper Concentrations. *Journal of the Marine Biological Association of the United Kingdom*, **65** (2), 421-431. DOI https://doi.org/10.1017/S0025315400050529

Rivera-Duarte, I., Rosen, G., Lapota, D., Chadwick, D.B., Kear-Padilla, L. & Zirino, A., 2005. Copper Toxicity to Larval Stages of Three Marine Invertebrates and Copper Complexation Capacity in San Diego Bay, California. *Environmental Science & Technology*, **39** (6), 1542-1546. DOI https://doi.org/10.1021/es040545j

Roberts, D., 1972. The Assimilation and Chronic Effects of Sub-lethal Concentrations of Endosulfan on Condition and Spawning in the Common Mussel *Mytilus edulis*. *Marine Biology*, **16** (2), 119-125. DOI https://doi.org/10.1007/BF00347949

Roberts, D., 1975. The Effect of Pesticides on Byssus Formation in the Common Mussel, *Mytilus edulis*. *Environmental Pollution (1970)*, **8** (4), 241-254. DOI https://doi.org/10.1016/0013-9327(75)90080-4

Rolan, G.R. & Gallagher, R., 1991. Recovery of intertidal biotic communities at Sullom Voe following the *Esso Bernica* oil spill of 1978. 1991 *Oil Spill Conference*, pp. 461-465.

Rosen, G., Rivera-Duarte, I., Bart Chadwick, D., Ryan, A., Santore, R.C. & Paquin, P.R., 2008. Critical tissue copper residues for marine bivalve (*Mytilus galloprovincialis*) and echinoderm (Strongylocentrotus purpuratus) embryonic development: Conceptual, regulatory and environmental implications. *Marine Environmental Research*, **66** (3), 327-336. DOI https://doi.org/10.1016/j.marenvres.2008.05.006

Rostron, D. & Bunker, F., 1997. An assessment of sublittoral epibenthic communities and species following the *Sea Empress* oil spill. *A report to the Countryside Council for Wales from Marine Seen & Sub-Sea Survey*.

Sabourin, T.D. & Tullis, R.E., 1981. Effect of three aromatic hydrocarbons on respiration and heart rates of the mussel, *Mytilus californianus*. *Bulletin of Environmental Contamination and Toxicology*, **26** (1), 729-736. DOI https://doi.org/10.1007/BF01622163

Saco-Alvarez, L., Bellas, J., Nieto, O., Bayona, J.M., Albaiges, J. & Beiras, R., 2008. Toxicity and phototoxicity of water-accommodated fraction obtained from Prestige fuel oil and marine fuel oil evaluated by marine bioassays. *Science of the Total Environment*, **394** (2-3), 275-282. DOI https://doi.org/10.1016/j.scitotenv.2008.01.045

Salazar, M. & Salazar, S., 1987. Tributyltin Effects on Juvenile Mussel Growth. *OCEANS'87*, IEEE, pp. 1504-1510.

Salazar, M. & Salazar, S., 1989. Acute Effects of (Bis) tributyltin Oxide on Marine Organisms. Summary of Work Performed 1981 to 1983. *NAVAL OCEAN SYSTEMS CENTER SAN DIEGO CA,* pp.

Salazar, M.H. & Salazar, S.M., 1991. ASSESSING SITE-SPECIFIC EFFECTS OF TBT CONTAMINATION WITH MUSSEL GROWTH-RATES. *Marine Environmental Research*, **32** (1-4), 131-150. DOI https://doi.org/10.1016/0141-1136(91)90038-a

Salazar, M.H. & Salazar, S.M., 1996. Mussels as Bioindicators: Effects of TBT on Survival, Bioaccumulation, and Growth Under Natural Conditions. In Champ, M.A. and Seligman, P.F. (eds.). *Organotin: Environmental fate and effects*, Dordrecht: Springer Netherlands, pp. 305-330.

Sanders, B.M., Martin, L.S., Nelson, W.G., Phelps, D.K. & Welch, W., 1991. Relationships between accumulation of a 60 kDa stress protein and scope-for-growth in *Mytilus edulis* exposed to a range of copper concentrations. *Marine Environmental Research*, **31** (2), 81-97. DOI https://doi.org/10.1016/0141-1136(91)90021-y

Schmidt, W., O'Rourke, K., Hernan, R. & Quinn, B., 2011. Effects of the pharmaceuticals gemfibrozil and diclofenac on the marine mussel (Mytilus spp.) and their comparison with standardized toxicity tests. *Marine Pollution Bulletin*, **62** (7), 1389-1395. DOI https://doi.org/10.1016/j.marpolbul.2011.04.043

Schmidt, W., Rainville, L.C., McEneff, G., Sheehan, D. & Quinn, B., 2014. A proteomic evaluation of the effects of the pharmaceuticals diclofenac and gemfibrozil on marine mussels (Mytilus spp.): evidence for chronic sublethal effects on stress- response proteins. *Drug Testing and Analysis*, **6** (3), 210-219. DOI https://doi.org/10.1002/dta.1463

Schmutz, A., Tremblay, R., Audet, C., Gagné, J.-P., Pelletier, É. & St-Louis, R., 2021. Under ice spills of conventional crude oil and diluted bitumen: Physiological resilience of the blue mussel and transgenerational effects. *Science of the Total Environment*, **779**, 146316. DOI https://doi.org/10.1016/j.scitotenv.2021.146316

Serrano, R., Hernandez, F., Pena, J., Dosda, V. & Canales, J., 1995. Toxicity of Bioconcentration of Selected Organophosphorus Pesticides in *Mytilus galloprovincialis* and Venus gallina. *Archives of Environmental Contamination and Toxicology*, **29** (3), 284-290. DOI https://doi.org/10.1007/BF00212491

Sif, J., Khalil, A., Abouinan, H., Rouhi, A. & Mokhliss, K., 2016. Effects of phthalates on the biology of the mussel *Mytilus galloprovincialis* (from the Atlantic Coast of El Jadida, Morocco). *Journal of Xenobiotics*, **6** (2), 39-40. DOI https://doi.org/10.4081/xeno.2016.6589

Smith, E., Wraige, E., Donkin, P. & Rowland, S., 2001. Hydrocarbon humps in the marine environment: Synthesis, toxicity, and aqueous solubility of monoaromatic compounds. *Environmental Toxicology and Chemistry*, **20** (11), 2428-2432. DOI http://doi.org/10.1002/etc.5620201105

Smith, J.E. ed., 1968. *'Torrey Canyon' Pollution and marine life.* Cambridge: Cambridge University Press.

Sole, M., Shaw, J.P., Frickers, P.E., Readman, J.W. & Hutchinson, T.H., 2010. Effects on feeding rate and biomarker responses of marine mussels experimentally exposed to propranolol and acetaminophen. *Analytical and Bioanalytical Chemistry*, **396** (2), 649-656. DOI https://doi.org/10.1007/s00216-009-3182-1

Spangenberg, J.V. & Cherr, G.N., 1996. Developmental effects of barium exposure in a marine bivalve (Mytilus californianus). *Environmental Toxicology and Chemistry*, **15** (10), 1769-1774. DOI https://doi.org/10.1002/etc.5620151018

Stefansson, E.S., Langdon, C.J., Pargee, S.M., Blunt, S.M., Gage, S.J. & Stubblefield, W.A., 2016. Acute effects of non-weathered and weathered crude oil and dispersant associated with the *Deepwater Horizon* incident on the development of marine bivalve and echinoderm larvae. *Environmental Toxicology and Chemistry*, **35** (8), 2016-2028. DOI https://doi.org/10.1002/etc.3353

Stenalt, E., Johansen, B., Lillienskjold, S.v. & Hansen, B.W., 1998. Mesocosm Study of*Mytilus edulis*Larvae and Postlarvae, Including the Settlement Phase, Exposed to a Gradient of Tributyltin. *Ecotoxicology and Environmental Safety*, **40** (3), 212-225. DOI https://doi.org/10.1006/eesa.1998.1687

Strømgren, T. & Bongard, T., 1987. The effect of tributyltin oxide on growth of *Mytilus edulis*. *Marine Pollution Bulletin*, **18** (1), 30-31. DOI https://doi.org/10.1016/0025-326x(87)90654-0

Strømgren, T. & Nielsen, M.V., 1986. Effect of diurnal variations in natural irradiance on the apical length growth and light saturation of growth in five species of benthic macroalgae. *Marine Biology*, **90**, 467-472.

Strømgren, T. & Nielsen, M.V., 1991. Spawning frequency, growth and mortality of *Mytilus edulis* larvae, exposed to copper and diesel oil. *Aquatic Toxicology*, **21** (3), 171-179. DOI https://doi.org/10.1016/0166-445X(91)90071-G

Strømgren, T., 1982. Effect of heavy metals (Zn, Hg, Cu, Cd, Pb, Ni) on the length growth of *Mytilus edulis*. *Marine Biology*, **72** (1), 69-72. DOI https://doi.org/10.1007/BF00393949

Strömgren, T., 1986. The combined effect of copper and hydrocarbons on the length growth of *Mytilus edulis*. *Marine Environmental Research*, **19** (4), 251-258. DOI https://doi.org/10.1016/0141-1136(86)90018-8

Sunila, I. & Lindström, R., 1985. Survival, growth and shell deformities of copper- and cadmium-exposed mussels (*Mytilus edulis* L.) in brackish water. *Estuarine, Coastal and Shelf Science*, **21** (4), 555-565. DOI https://doi.org/10.1016/0272-7714(85)90056-3

Sunila, I. & Lindström, R., 1986. Effects of copper and cadmium on the shell morphology, length growth and survival of the mussel *Mytilus edulis* L. *Publications of the Water Research Institute, National Board of Waters, Finland*, **68**, 211-214.

Sunila, I., 1981. Toxicity of copper and cadmium to *Mytilus edulis* L. (Bivalvia) in brackish water. *Annales Zoologici Fennici*, **18**, 213-223.

Swedmark, M., Granmo, Å. & Kollberg, S., 1973. Effects of oil dispersants and oil emulsions on marine animals. *Water Research*, **7** (11), 1649-1672. DOI https://doi.org/10.1016/0043-1354(73)90134-6

Talbot, V., Magee, R.J. & Hussain, M., 1976. Lead in Port Phillip Bay mussels. *Marine Pollution Bulletin*, **7** (12), 234-237. DOI https://doi.org/10.1016/0025-326X(76)90269-1

Tedengren, M., Olsson, B., Bradley, B. & Zhou, L.Z., 1999b. Heavy metal uptake, physiological response and survival of the blue mussel (*Mytilus edulis*) from marine and brackish waters in relation to the induction of heat-shock protein 70. *Hydrobiologia*, **393**, 261-269. DOI https://doi.org/10.1023/a:1003583509218

Tedesco, S., Doyle, H., Blasco, J., Redmond, G. & Sheehan, D., 2010. Exposure of the blue mussel, *Mytilus edulis*, to gold nanoparticles and the pro-oxidant menadione. *Comparative Biochemistry and Physiology Part C: Toxicology & Pharmacology*, **151** (2), 167-174. DOI https://doi.org/10.1016/j.cbpc.2009.10.002

Thomas, R.E., Brodersen, C., Carls, M.G., Babcock, M. & Rice, S.D., 1999. Lack of physiological responses to hydrocarbon accumulation by *Mytilus trossulus* after 3–4 years chronic exposure to spilled Exxon Valdez crude oil in Prince William Sound. *Comparative Biochemistry and Physiology Part C: Pharmacology, Toxicology and Endocrinology*, **122** (1), 153-163. DOI https://doi.org/10.1016/S0742-8413(98)10099-3

Thurberg, F.P., Calabrese, A. & Dawson, M.A., 1974. Effects of silver on oxygen consumption of bivalves at various salinities. In Vernberg, J.F. and Vernberg, W.B. (eds.). *Pollution and Physiology of Marine Organisms*, New York: Academic Press, pp. 67-78.

Tuffnail, W., Mills, G.A., Cary, P. & Greenwood, R., 2009. An environmental 1H NMR metabolomic study of the exposure of the marine mussel *Mytilus edulis* to atrazine, lindane, hypoxia and starvation. *Metabolomics*, **5** (1), 33-43. DOI https://doi.org/10.1007/s11306-008-0143-1

Valkirs, A.O., Davidson, B.M. & Seligman, P.F., 1987. Sublethal growth effects and mortality to marine bivalves from long-term exposure to tributyltin. *Chemosphere*, **16** (1), 201-220. DOI https://doi.org/10.1016/0045-6535(87)90124-X

Vlachogianni, T. & Valavanidis, A., 2007. Heavy-Metal Effects on Lipid Peroxidation and Antioxidant Defence Enzymes in Mussels *Mytilus galloprovincialis*. *Chemistry and Ecology*, **23**, 361-371. DOI https://doi.org/10.1080/02757540701653285

Walsh, A.R. & Ohalloran, J., 1997. The toxicity of leather tannery effluent to a population of the blue mussel *Mytilus edulis* (L). *Ecotoxicology*, **6** (3), 137-152. DOI https://doi.org/10.1023/a:1018614408367

Weber, R.E., Dezwaan, A. & Bang, A., 1992. Interactive Effects of Ambient Copper and Anoxic, Temperature and Salinity Stress on Survival and Hemolymph and Muscle Tissue Osmotic Effectors in *Mytilus edulis*. *Journal of Experimental Marine Biology and Ecology*, **159** (2), 135-156. DOI https://doi.org/10.1016/0022-0981(92)90033-7

Widdows, J. & Donkin, P., 1992. Mussels and environmental contaminants: bioaccumulation and physiological aspects. . In Gosling, E.M. (ed.) *The mussel Mytilus: ecology, physiology, genetics and culture*, Amsterdam: Elsevier Science Publ. 383-424 pp. [[Developments in Aquaculture and Fisheries Science, no. 25], 25].

Widdows, J. & Johnson, D., 1988. Physiological energetics of *Mytilus edulis*: scope for growth. *Marine Ecology Progress Series*, **46**, 113-121. DOI https://doi.org/https://www.int-res.com/articles/meps/46/m046p113.pdf

Widdows, J. & Page, D.S., 1993. Effects of tributyltin and dibutyltin on the physiological energetics of the mussel, *Mytilus edulis*. *Marine Environmental Research*, **35** (3), 233-249. DOI https://doi.org/10.1016/0141-1136(93)90096-i

Widdows, J., Bakke, T., Bayne, B.L., Donkin, P., Livingstone, D.R., Lowe, D.M., Moore, M.N., Evans, S.V. & Moore, S.L., 1982. Responses of *Mytilus edulis* on exposure to the water-accommodated fraction of North Sea oil. *Marine Biology*, **67** (1), 15-31. DOI https://doi.org/10.1007/BF00397090

Widdows, J., Donkin, P. & Evans, S.V., 1987. Physiological responses of *Mytilus edulis* during chronic oil exposure and recovery. *Marine Environmental Research*, **23** (1), 15-32. DOI https://doi.org/10.1016/0141-1136(87)90014-6

Widdows, J., Donkin, P., Brinsley, M.D., Evans, S.V., Salkeld, P.N., Franklin, A., Law, R.J. & Waldock, M.J., 1995. Scope for growth and contaminant levels in North-Sea mussels *Mytilus edulis*. *Marine Ecology Progress Series*, **127** (1-3), 131-148. DOI https://doi.org/10.3354/meps127131

Widdows, J., Donkin, P., Staff, F.J., Matthiessen, P., Law, R.J., Allen, Y.T., Thain, J.E., Allchin, C.R. & Jones, B.R., 2002. Measurement of stress effects (scope for growth) and contaminant levels in mussels (*Mytilus edulis*) collected from the Irish Sea. *Marine Environmental Research*, **53** (4), 327-356. DOI https://doi.org/10.1016/s0141-1136(01)00120-9

Yang, J.L., Li, Y.F., Bao, W.Y., Satuito, C.G. & Kitamura, H., 2011. Larval metamorphosis of the mussel *Mytilus galloprovincialis* Lamarck, 1819 in response to neurotransmitter blockers and tetraethylammonium. *Biofouling*, **27** (2), 193-199. DOI https://doi.org/10.1080/08927014.2011.553717

Yang, J.-L., Li, W.-S., Liang, X., Li, Y.-F., Chen, Y.-R., Bao, W.-Y. & Li, J.-L., 2014. Effects of Adrenoceptor Compounds on Larval Metamorphosis of the Mussel Mytilus coruscus. *Aquaculture*, **426**, 282-287. DOI https://doi.org/10.1016/j.aquaculture.2014.02.019

Yaroslavtseva, L.M. & Sergeeva, E.P., 2007. Effect of temperature on early development of the pacific mussel *Mytilus trossulus* (Bivalvia: Mytilidae) in sea water polluted by copper ions. *Russian Journal of Marine Biology*, **33** (6), 375-380. DOI https://doi.org/10.1134/s106307400706003x