



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:

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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 spills¹ (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

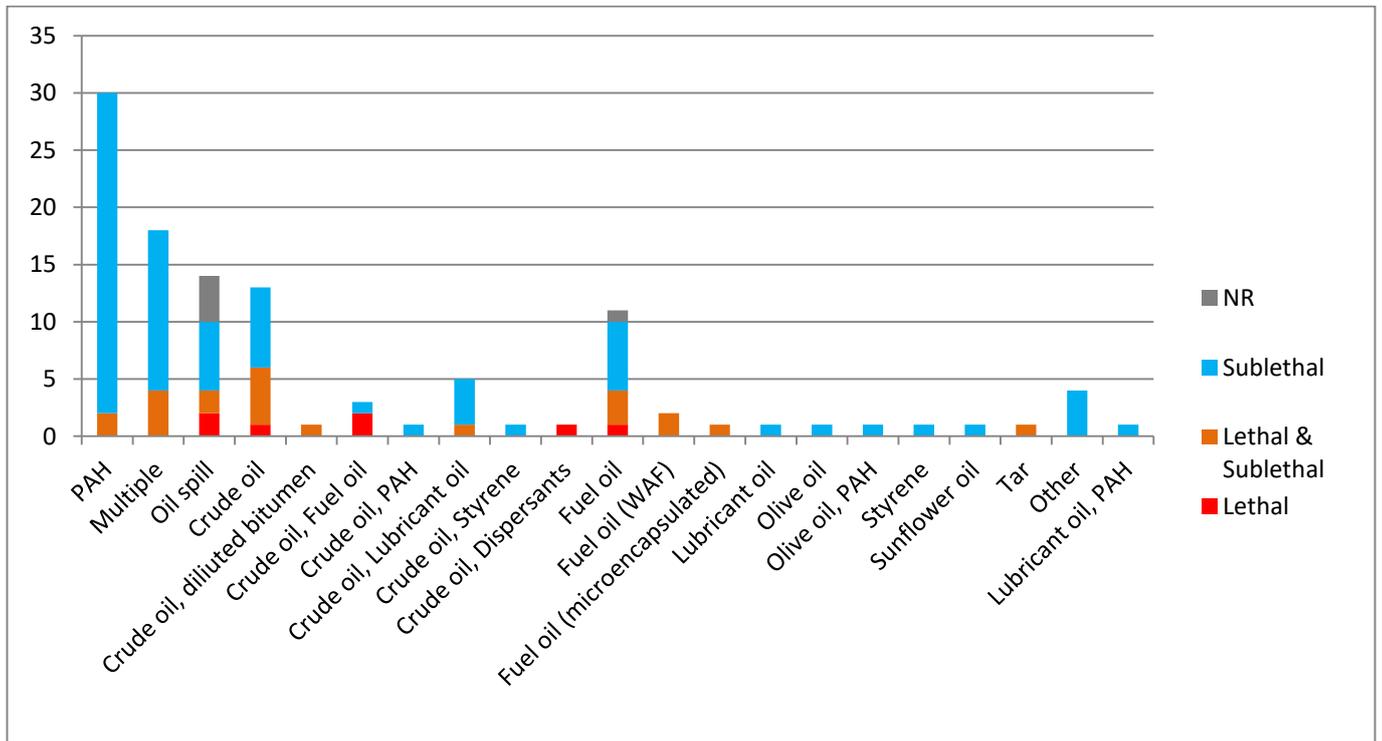


Figure 1.1. Number of articles examined that reported lethal and sub-lethal effects to a range of hydrocarbon contaminants in *Mytilus* spp. (NR= not reported).

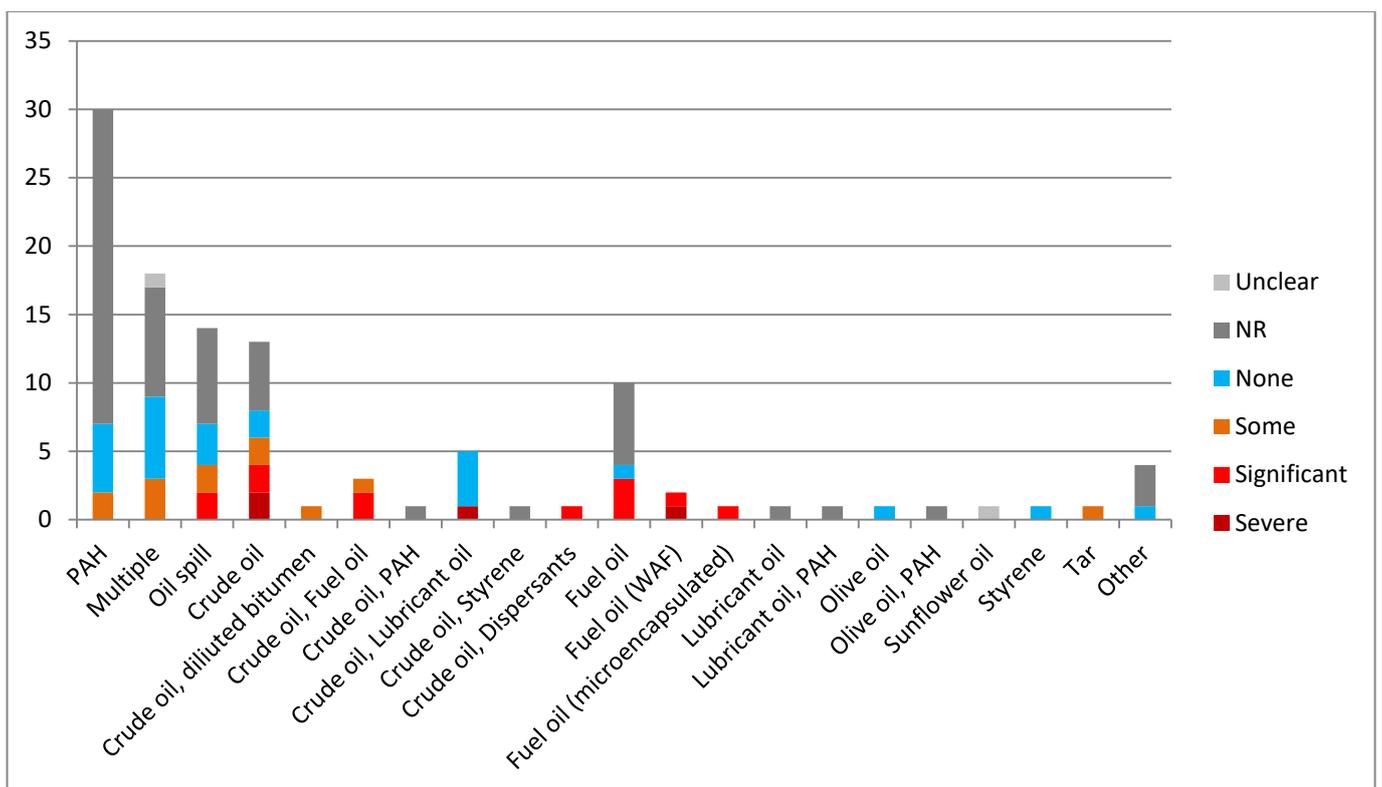


Figure 1.2. Count of ranked mortality (from 'severe' to 'none') in articles examined to a range of hydrocarbon contaminants in *Mytilus* spp. (NR= not reported).

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 LC₅₀, LT₅₀, or EC₅₀ 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 LC₅₀ or LT₅₀ 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 EC₅₀ (50% larval abnormalities 48 hours) was 13% WAF irrespective of light regime, while the EC₅₀ was 20% Marine WAF in the light treatment and >100% in darkness EC₅₀. 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 LC₅₀ after 96 hr exposure to Oman crude oil and 48 hr recovery in clean seawater was >1000 ppm.

Table 1.2. Examples of LC₅₀, LT₅₀, or EC₅₀ values for the effects of oils on *Mytilus* 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 <i>et al.</i> , 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 <i>et al.</i> , 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 <i>et al.</i> , 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 <i>et al.</i> , 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)	Strømngren & Nielsen, 1991; His <i>et al.</i> , 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 LC₅₀ (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 EC₁₀ values between echinoderm and bivalve larvae. The average EC₁₀ (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 LC₅₀ values for *Mytilus* larvae of ca 130² 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 *Mytilus* adults was around 40% when exposed to 5,000 µg/l microencapsulated diesel oil, with the LC₅₀ (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 LC₅₀ 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 EC₅₀ (10-day) of 24-30 µg/l; an order of magnitude less than the EC₅₀ for growth of juvenile mussels (ca 1000 µg/l; Strømngren & Reisen, 1988 unsee). 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 atretic³ 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 within 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 EC₅₀ embryogenesis of 2,000 µg /l, and 5-day LC₅₀ 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 LC₅₀ (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 EC₅₀ (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 EC₅₀ (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 LC₅₀ 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 LT₅₀s based on their 'survival in air'. Donkin *et al.* (1989) reported the EC₅₀ (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 phenanthrene (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 LT₅₀ values in the range of 3-4 days, while control treatment mussels had an LT₅₀ values of 7 days. The mussels from the PAH treatments also had lower cell viability, increased lysosomal acid phosphatase 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 LT₅₀ in air to examine the stress of the mussels. Although a highly polluted site, the mussels from Arriluze had a higher survival in air than those from 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' (LT₅₀) 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% (TEC₅₀). 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 Acetylcholinesterase (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 LC₅₀ 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.

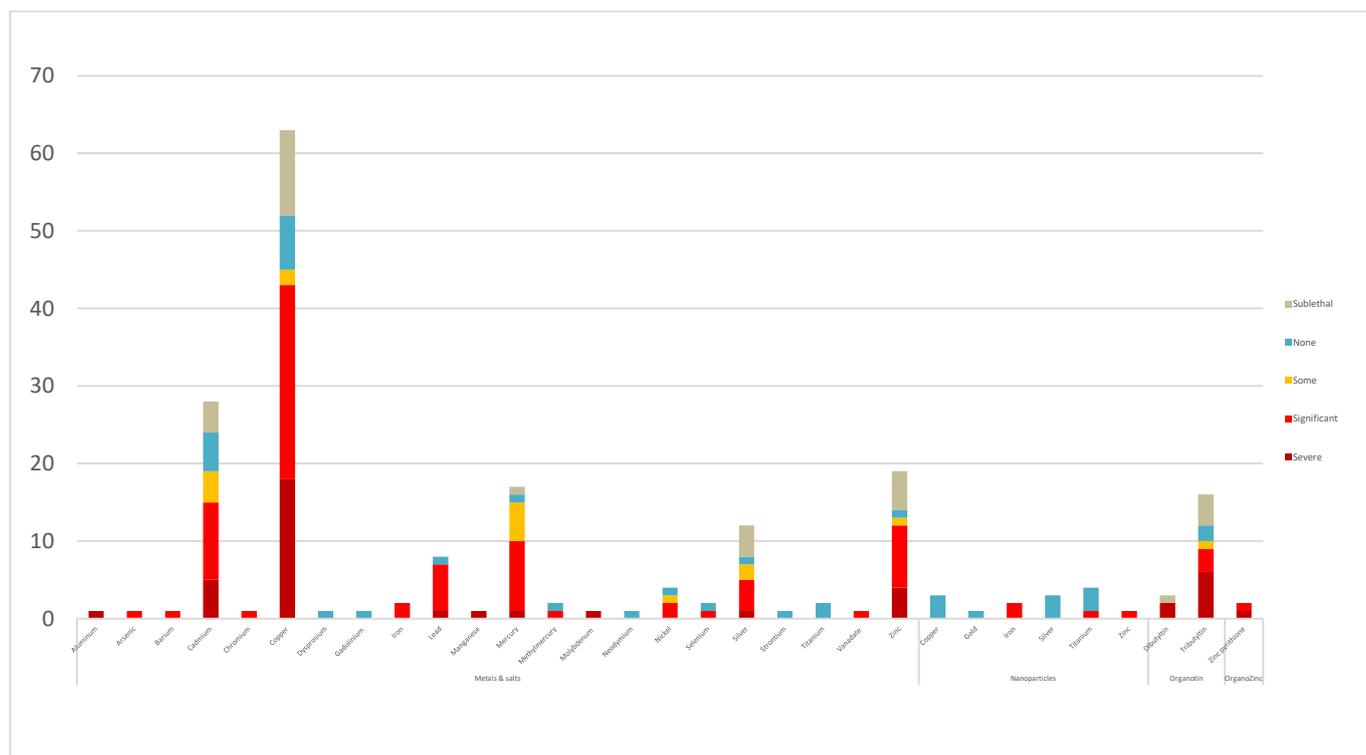


Figure 1.3. Count of ranked mortality (from 'severe' to 'none') in the articles examined for a range of metal contaminants in *Mytilus* spp..

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).

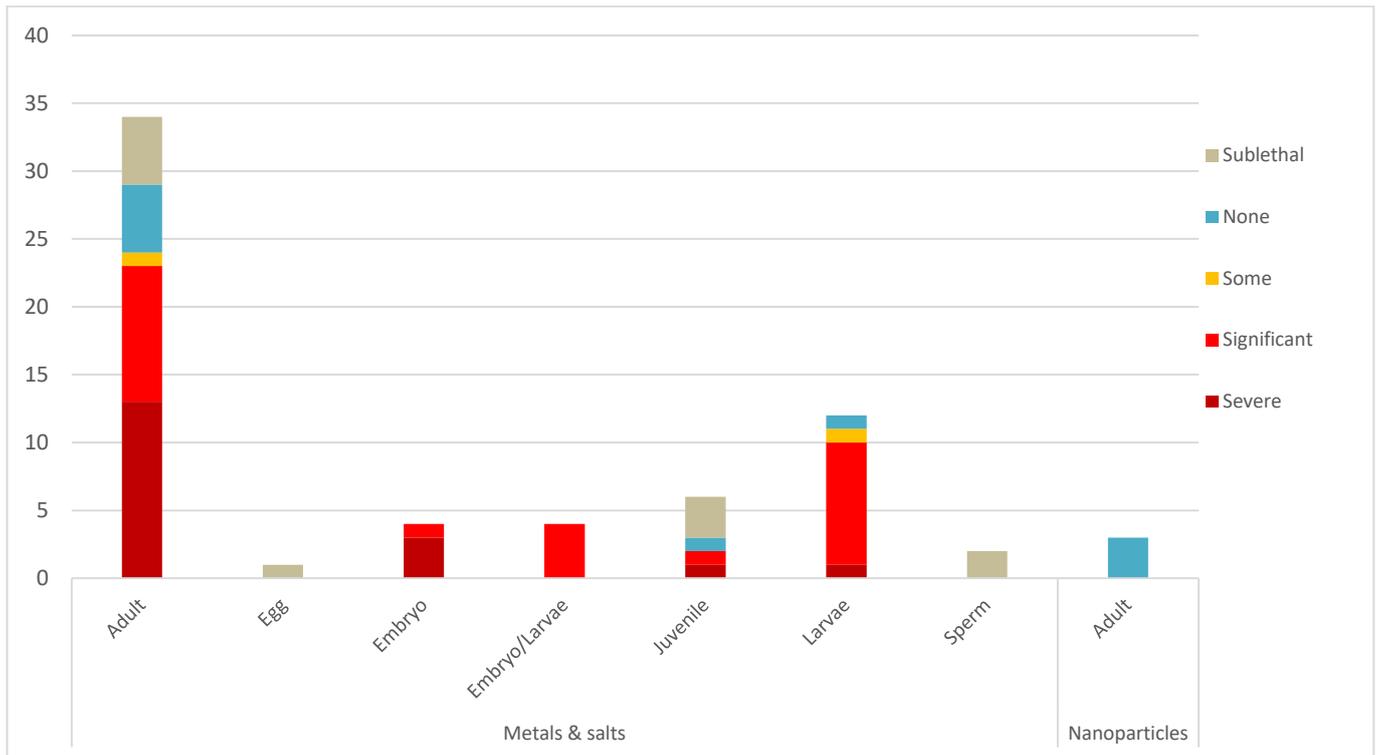


Figure 1.4. Count of ranked mortality (from 'severe' to 'none') in the articles examined for inorganic copper and its compounds in *Mytilus* spp..

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).

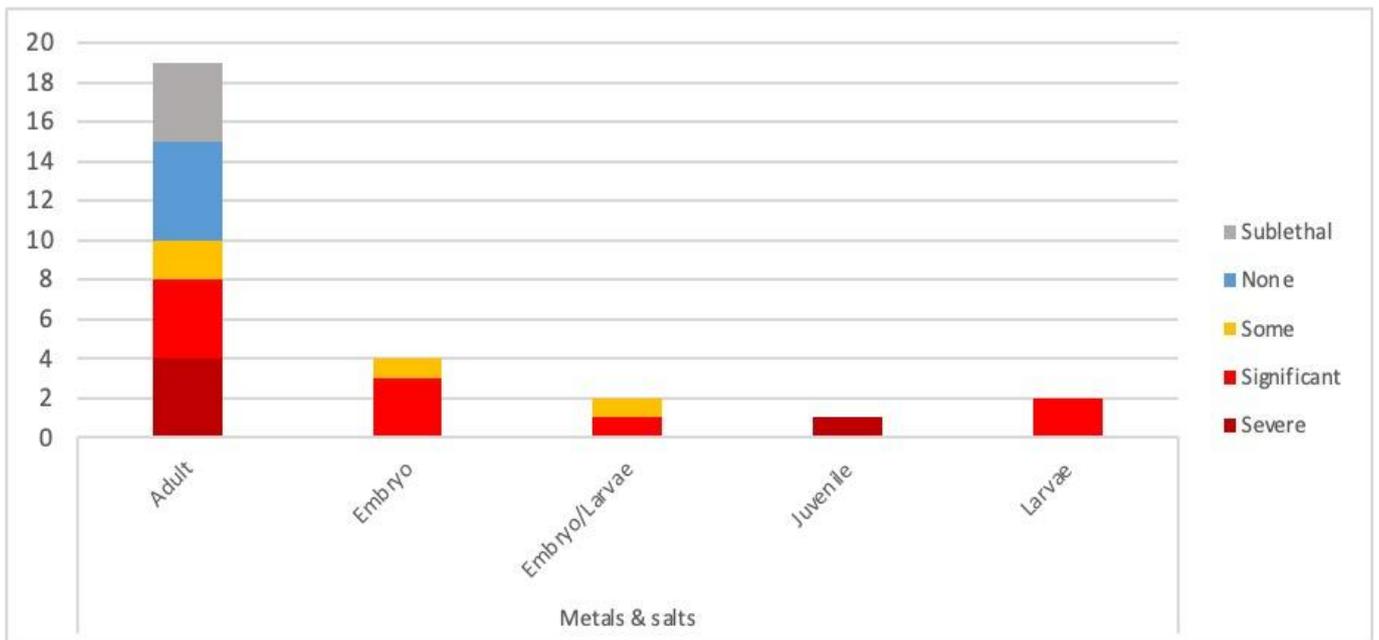


Figure 1.5. Count of ranked mortality (from 'severe' to 'none') in the articles examined for inorganic cadmium and its compounds. (NR= not reported).

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 (LC₅₀, 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 LC₅₀ >200 mg/l; 48-hour LC₅₀ 165 mg/l, and 96-hour LC₅₀ 25 mg/l.
- Vlahogianni & Valavandis (2007) conducted short-term toxicity tests with cadmium on *Mytilus galloprovincialis* adults establishing a 24-hour LC₅₀ 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 LC₅₀ 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 LC₅₀ 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 EC₅₀ 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 EC₅₀ 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 Cd²⁺ 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 Cd²⁺ 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 EC₅₀ 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 LC₅₀ 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.

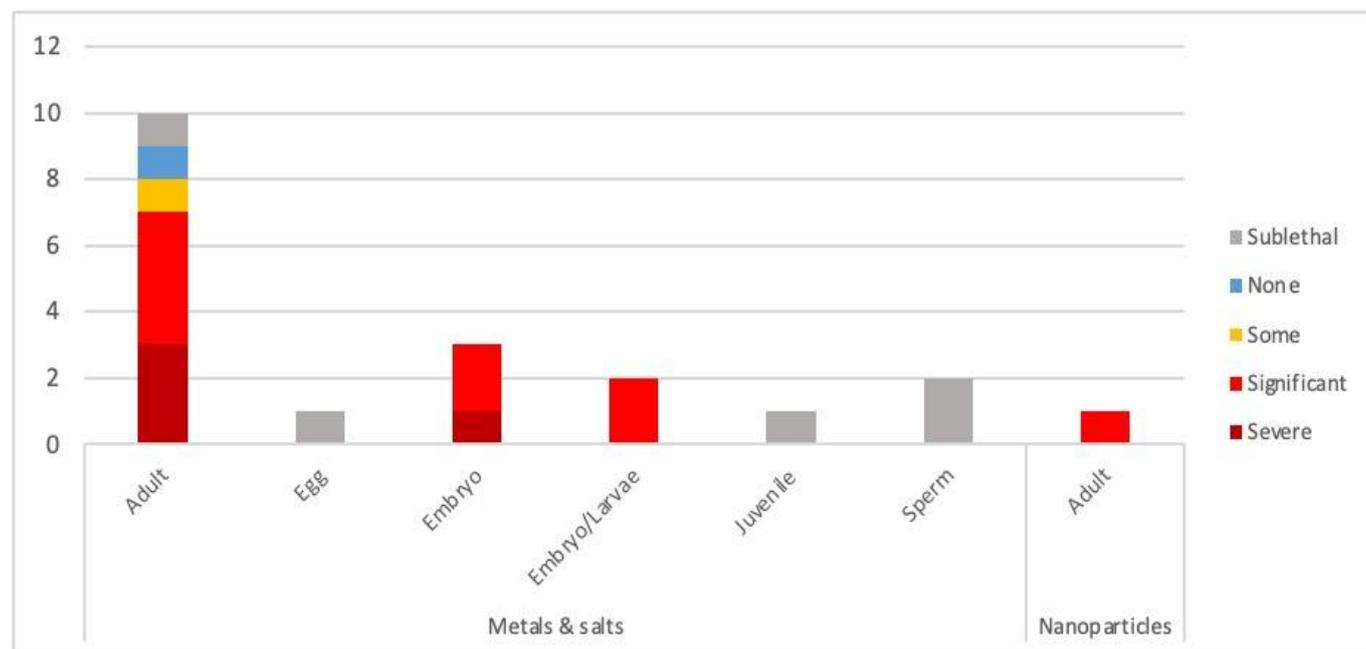


Figure 1.6. Count of ranked mortality (from 'severe' to 'none') in the articles examined for inorganic zinc and its compounds. (NR= not reported).

- 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 (ZnCl₂) 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 (LC₅₀) 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 LC₅₀ was estimated to be 7,800 µg/l (7.8 mg/l) after 96 hours.
- Hietanen *et al.* (1988) found the LC₅₀ value of zinc on *Mytilus edulis* to be 20.8 mg/l during a 41-day exposure. Throughout the experiment, the LC₅₀ 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 EC₅₀ of 150 µg/l (0.15 mg/l) and an EC₂₀ 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 EC₅₀ 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 EC₅₀ 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 EC₅₀ 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 LC₅₀ of 2500 µg/l (2.5 mg/l) zinc in static exposure trials, and LC₅₀s 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).

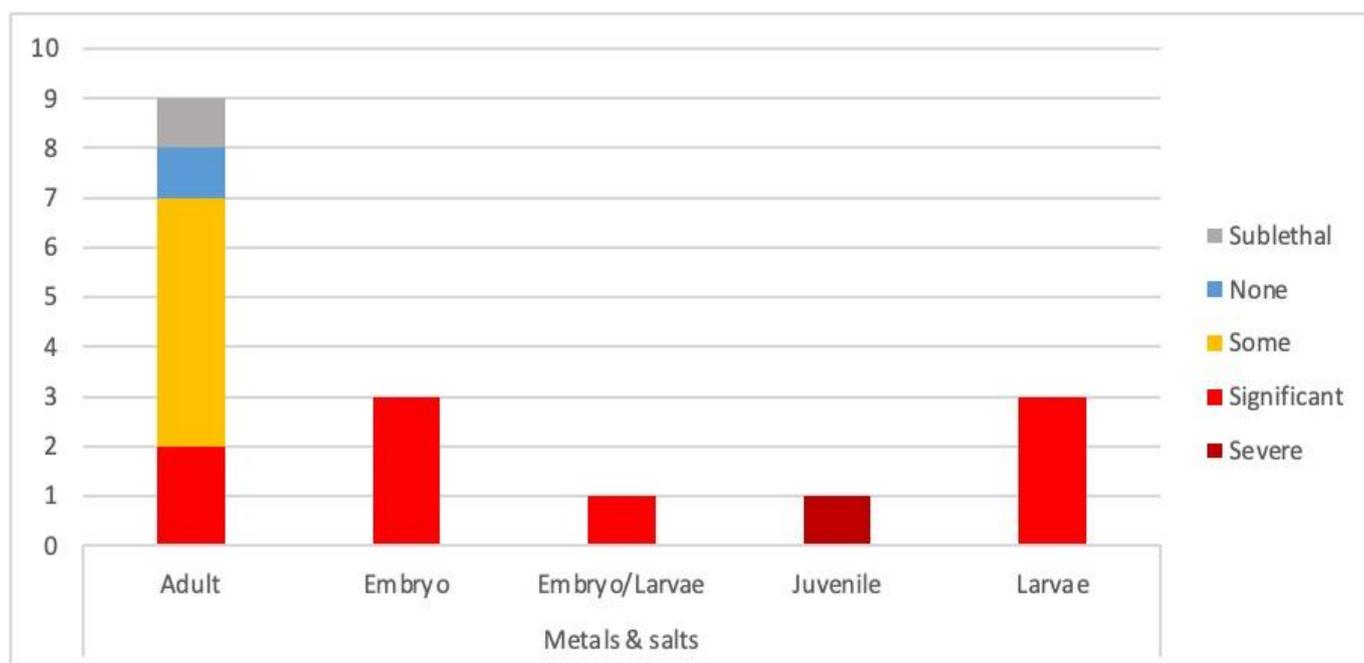


Figure 1.7. Count of ranked mortality (from 'severe' to 'none') in the articles examined for inorganic mercury and its compounds.

- 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 LC₅₀ and LC₉₅ 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 EC₅₀ 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 EC₅₀ 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 EC₅₀ 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 LC₅₀s 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 EC₅₀ 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 EC₅₀ 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 EC₅₀ 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 LC₅₀ 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 EC₅₀ 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) LT₅₀ 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 LC₅₀ 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 EC₅₀ 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).

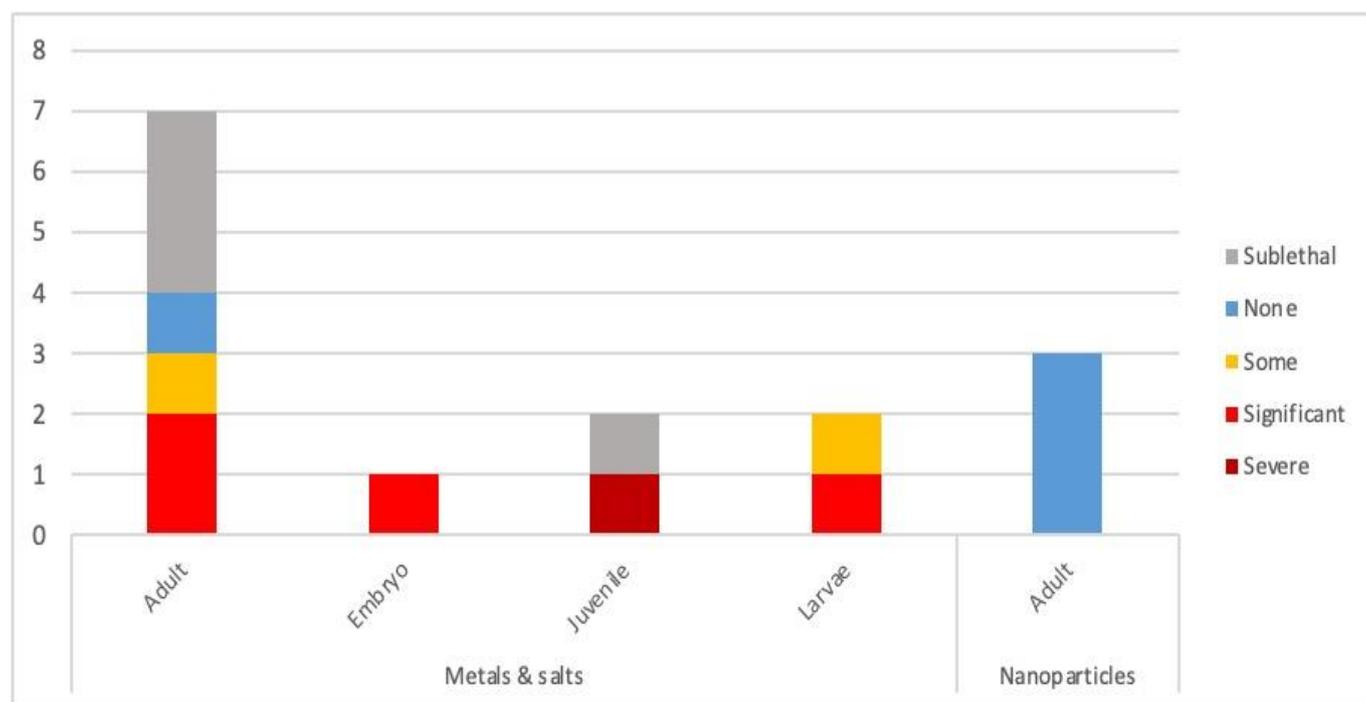


Figure 1.8. Count of ranked mortality (from 'severe' to 'none') in the articles examined for inorganic silver and its compounds.

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 LC₅₀ 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: LD₅₀ 20 mg/l 40 days; LD₅₀ 30 mg/l 30-40 days; LD₅₀ 10-20 mg/l 50-100 days; and LD₅₀ 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.

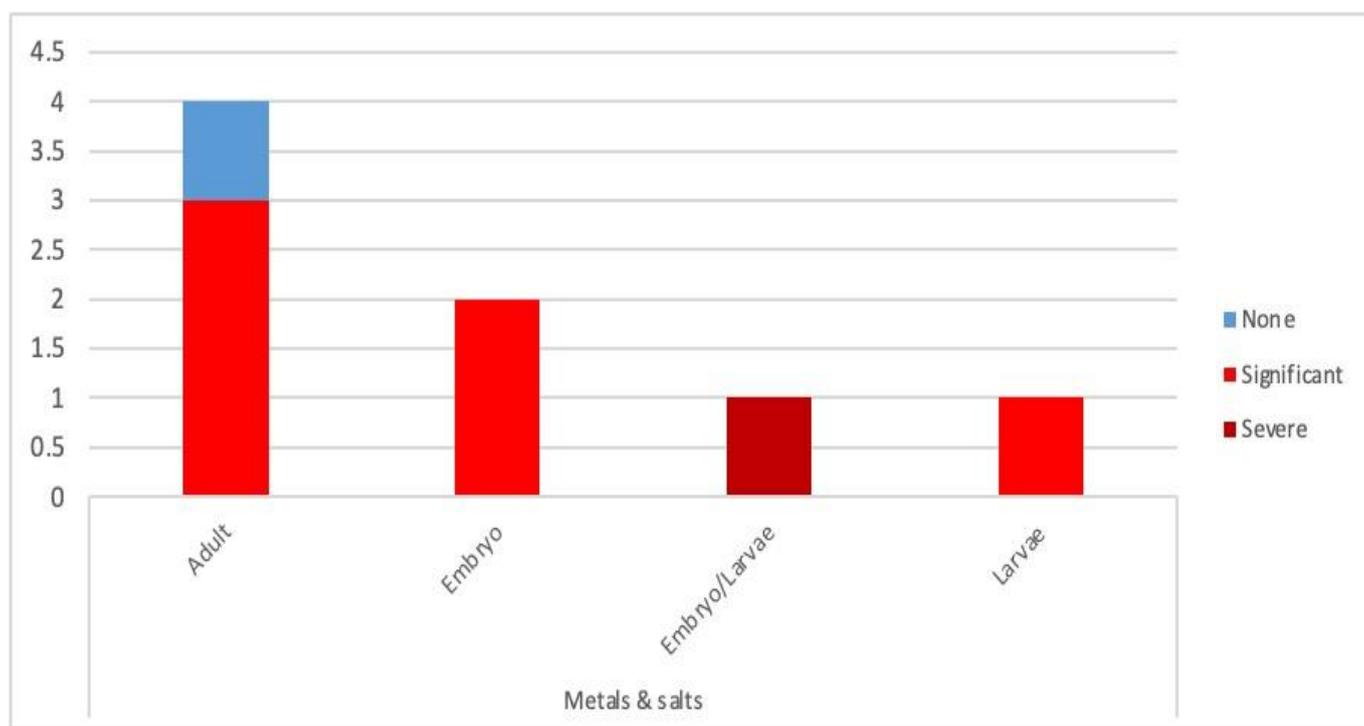


Figure 1.9. Count of ranked mortality (from 'severe' to 'none') in the articles examined for inorganic lead and its compounds.

- 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 EC₅₀ 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 EC₅₀ of 150 µg/l (0.15mg/l) and an EC₂₀ 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 EC₅₀ 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 & Schlekot (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_{10S} (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 LC₅₀ 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 EC₅₀ 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 $\text{Al}_2(\text{SO}_4)_3$ at concentrations $\geq 10^{-6}$ M. At a concentration of 3×10^{-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 $\mu\text{g/l}$ (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 $\mu\text{g/l}$ (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 $\mu\text{g/l}$ (4.469 mg/l).

Dysprosium. Freitas *et al.* (2020a) found 28-day exposures to a variety of concentrations of dysprosium up to 40 $\mu\text{g/l}$ (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 $\mu\text{g/l}$ (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 $\mu\text{g/l}$ (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 $\mu\text{g/l}$ (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 LC₅₀ 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 LC₅₀ value. The results of the exposure treatment produced an LC₅₀ of 0.97 µg/l TBT, which is considerably lower than 96-hour LC₅₀ 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. Avelas *et al.* (2017) investigated the effects of zinc pyrithione on adult mussels and reported a 96-hour LC₅₀ 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 (EC₁₀). 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 EC₅₀).

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-TiO₂ 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-TiO₂ 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-TiO₂) 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 EC₅₀ 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 nanoparticles. 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 nanoparticles. 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)

Group	Contaminant	Mortality (worst case reported)						Assessment			
		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	M⁵
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	H⁶
OrganoZinc											
	Zinc pyrithione	1						1	N	L	H
Grand Total		26	29	11	34	26	4	130	N	L	H⁷

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)

Group	Contaminant	Mortality (worst case reported)						Assessment			
		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.

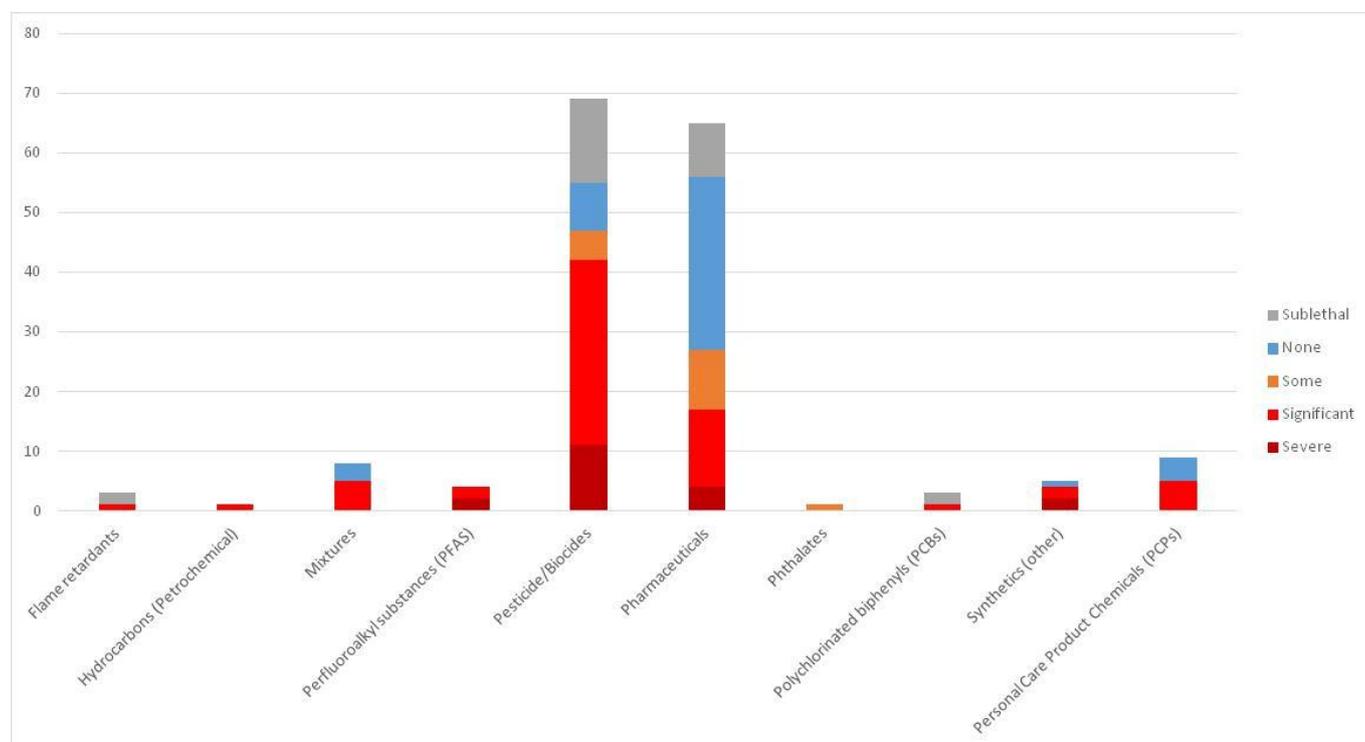


Figure 1.10. Count of ranked mortality due to exposure to synthetic contaminants in *Mytilus* spp.. Mortality is ranked as follows: 'Severe' (>75%), 'Significant' (25-75%), 'Some' (<25%), 'None' (no mortality reported), and 'Sublethal' effects. Note some articles are included more than once because they 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 EC₅₀ 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 EC₅₀ 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 LC₅₀s, 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 EC₂₀ and EC₅₀ that resulted in abnormal larvae development were 0.94 and 1.1 mg/l, respectively. Complete (100%) mortality occurred at >2mg/l PFOS, with LC₂₀ and LC₅₀ values determined at 0.93 and 1.07 mg/l, respectively. For PFOA the EC₂₀ and EC₅₀ that resulted in abnormal larvae development were 3.47 and 12 mg/l, respectively. Complete (100%) mortality occurred at 52 mg/l PFOA with LC₂₀ and LC₅₀ 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 (EC₅₀ 587.17 µg/l), then, with similar toxicity, EHMC (EC₅₀ 3118.19 µg/L) and then BP-3 (EC₅₀ 3472.59 µg/l). BP-4 was not toxic at the tested concentrations, with an EC₅₀ 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 EC₅₀ of Ethylhexyl Dimethyl p-Aminobenzoic Acid were 25, 100, and 130 µg/l, respectively. The established NOEC, LOEC and EC₅₀ 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 LC₅₀ values for Dieldrin at 14 and 30 days of exposure were >200 µg/l and 180 µg/l, respectively. The LC₅₀ values for pentachlorophenol at 4, 7, and 14 days exposure were 18,000 µg/l, 950 µg/l and 750 µg/l, respectively. The LC₅₀ 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 EC₅₀ 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 EC₅₀ 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 EC₅₀ values of Sevin on the larval developmental stages ranged from 5.3 to 24 mg/l, and the EC₅₀ of Sevin on the unfertilized egg was 20.7 mg/l.

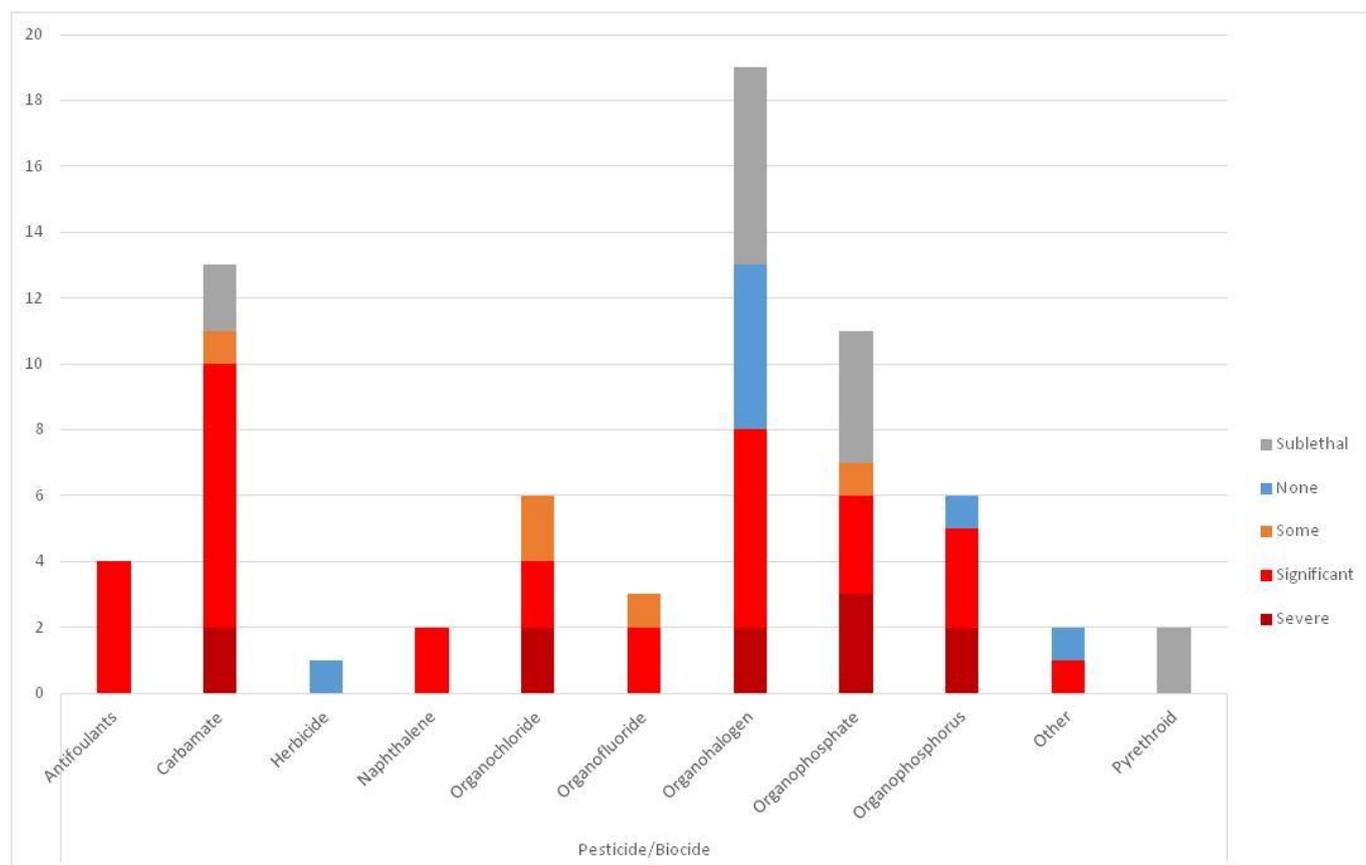


Figure 1.11. Count of ranked mortality due to exposure to pesticides or biocides in *Mytilus* spp.. Mortality is ranked as follows: 'Severe' (>75%), 'Significant' (25-75%), 'Some' (<25%), 'None' (no mortality reported), and 'Sublethal' effects. Note some articles are included more than once because they 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 EC₁₀ and EC₅₀ 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 EC₅₀ (median effective concentration) and EC₁₀ reducing embryogenesis success, larval growth, and larval settlement by 50% and 10% respectively. Chlorothalonil produced EC₁₀ and EC₅₀ values of 4.5 and 8.8 µg/l, whilst 'Sea-Nine 211' values were 7.1 and 11 µg/l. Dichlofluanid and Tolyfluanid showed similar toxicity, with EC₁₀ values of 52 and 49 µg/l and EC₅₀ values of 81 and 74 µg/l, respectively. Irgarol 1051 was the least toxic biocide with EC₁₀ and EC₅₀ of 797 and 1,540 µg/l. Sea-Nine 211 and Chlorothalonil were approximately 6–7 times more toxic than Dichlofluanid and Tolyfluanid, 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 LC₅₀ 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 LC₅₀ 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 LT₅₀ values were established. The control group had an LT₅₀ of 5.14 days whilst the mussels that had been exposed to 1 and 2 mg/l Atrazine had LT₅₀s 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 EC₅₀ 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 EC₅₀ of 1.69 mg/l. Dichlorvos also affected the survival of *Mytilus edulis*, with a 24-hour LC₅₀ of 8.2 mg/l.
- Pena-Llopis *et al.* (2002) investigated the toxicity of Fenitrothion and established 96-hour LC₅₀ and LC₈₅ 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 LC₅₀ 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 LC₅₀ values were calculated for each of the contaminants based on the survival of adults, and 48-hour EC₅₀ values were calculated based on larval developmental abnormalities (Table 1.6).

Table 1.6. 96-hour EC₅₀s and LC₅₀ 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 agents⁸ (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 (Propranolol⁹ (PROP), 17- α ethinylestradiol¹⁰ (EE2), and Gemfibrozil¹¹ (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 μ g/l), EE2 (0.005, 0.05, 0.5 μ g/l), and GEM (0.050, 0.500, 5 μ g/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 μ g/l) and GEM (5 μ g/l), and EC₁₀ values of 0.142 and 2.4 μ g/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 μ g/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 μ g/l EE2, with an EC₁₀ of 0.0025 μ g/l. The percentage of normally developed larvae was reduced by 23.3% at 0.5 μ g/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 EC₅₀ of 206.80 μ g/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

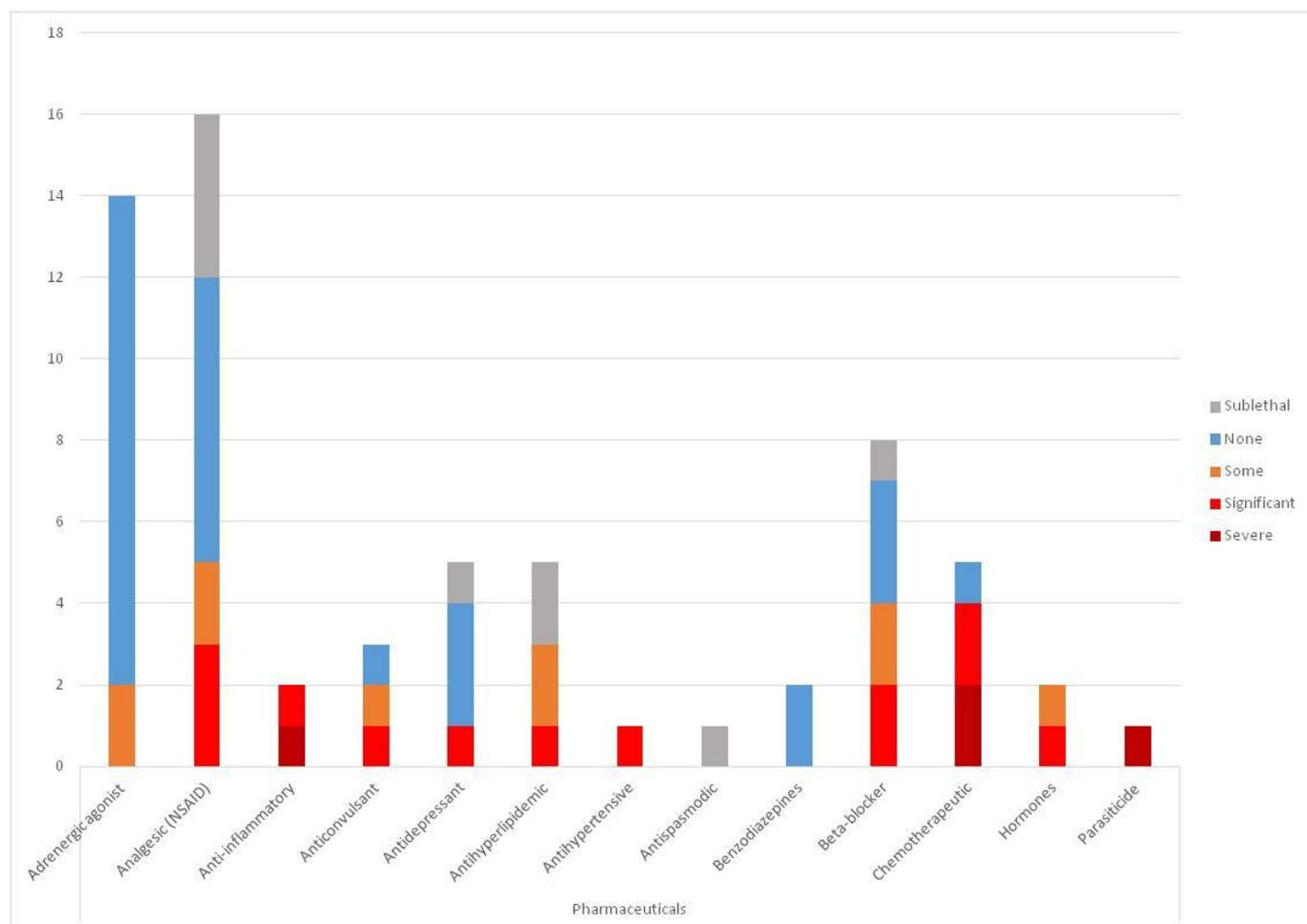


Figure 1.12. Count of ranked mortality due to exposure to pharmaceuticals in *Mytilus* spp.. Mortality is ranked as follows: 'Severe' (>75%), 'Significant' (25-75%), 'Some' (<25%), 'None' (no mortality reported), and 'Sublethal' effects. Note some articles are included more than once because they examined 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 Ibuprofen¹² and Bezafibrate¹³ 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. Diclofenac¹⁴ 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 Carbamazepine¹⁵ 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 EC₅₀s 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 Buscopan¹⁶ plus and Mesulid¹⁷ 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 LT₅₀ 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 IC₅₀ 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 LT₅₀ values for their survival in air. Mortalities were low (<5%) during the seven weeks exposure period. However, 50% mortality (LT₅₀) 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 LC₅₀ 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 LC₅₀ 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 EC₅₀ 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 LT₅₀s 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), 17 α -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 LC₅₀ 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 in 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 in 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).

Group	Contaminant	Mortality (worst case reported)						Assessment			
		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).

Group	Contaminant	Mortality (worst case reported)						Assessment			
		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

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