Pharmaceutical pollution of marine environments has important biological consequences for aquatic organisms. This study investigated the effects on mussels of treatment with environmentally relevant levels of an antidepressant, fluoxetine, and a beta-blocker, propranolol, using biomarkers including DNA damage. The results showed that mussels are most vulnerable to these drugs in combination.

Many human pharmaceuticals are not completely broken down by the body, nor completely degraded by wastewater treatment, which means residues can be released into aquatic ecosystems. These residues can have negative effects on aquatic organisms, including changes to reproductive behaviour and physiology.

While many studies have investigated pharmaceutical pollution of freshwaters, comparatively few have studied the effects of pharmaceuticals in marine environments, as the dilution of larger bodies of water is assumed to reduce the risk. However, pharmaceutical residues do pose a risk in marine environments. Many are adsorbed to the sediment at the bottom of the water and to the solids suspended in the water. Organisms that live at the bottom of the water and feed on suspended materials may therefore be at particular risk.

This study investigated one such species, the Mediterranean mussel (*Mytilus galloprovincialis*), which lives at the water-sediment interface and filters large volumes of suspended material. This species can accumulate pollutants through its gills and digestive tract.

The researchers investigated the effects of two drugs: fluoxetine, an antidepressant better known as Prozac, and propranolol, a beta-blocker used to treat heart problems and high blood pressure. Both drugs have been detected in coastal environments.

The researchers, as part of the EU MEECE project, applied a multi-biomarker approach to investigate the effects of the drugs alone and in combination. In humans, these medications are contraindicated. This means they should not be taken together, because fluoxetine may potentiate the effect of propranolol, causing dangerously low blood pressure for example.

The mussels were administered propranolol and fluoxetine alone and in combination, at environmentally relevant concentrations of 0.3 ng/l, daily for seven days.

After the seven-day treatment, the authors sampled gills, digestive gland and haemolymph and assessed the health of the pharmaceutical-treated mussels compared to a control group. The authors used multiple biomarkers to measure the health of the mussels, including the activity of the part of the cell responsible for breaking down waste materials (the lysosome), expression of antioxidant enzymes, and DNA damage.

Information from these different biomarkers was integrated using the Mussel Expert System, which provides a clear indication of the stress induced by pollutants in mussels. The system provides ‘Health Status Index’ levels of healthy, low stress, medium stress, high stress, or pathological stress.

Continued on next page.
Combined, the drugs caused medium stress in mussels, although either drug alone did not induce consistent stress. The ability to degrade waste material, measured by lysosomal parameters, was significantly impaired, but there was no significant effect on antioxidant response or levels of DNA damage. Co-exposure also facilitated the bioaccumulation of propranolol, as the compound only accumulated in the digestive gland of mussels treated with both compounds.

The co-treatment of mussels with fluoxetine and propranolol at environmentally relevant levels increased stress levels in the mussels, showing a new susceptibility of marine and coastal organisms to pharmaceuticals. While past studies have shown that these drugs can affect invertebrate species, this is one of the first to suggest that they may also affect mussels and other bivalves, such as oysters and scallops. The authors say the drugs may affect the ability of bivalves to cope with other stressors and therefore jeopardise their fitness within natural populations.

The evaluation of biomarkers in environmentally relevant species like marine mussels is a promising method of assessing the risks posed by pharmaceuticals, and other anthropogenic chemicals, in coastal environments. This work will support the use of mussels as a monitoring tool in coastal environments.