

# Plasticisers

Three drugs have been recalled after tests indicated the presence of plasticisers DEHP and DIDP. Recent press coverage on the presence of DEHP and DIDP in food and pharmaceutical products has aroused the public's attention. What are they and how are they used? Is there evidence of health concerns and human harm with DEHP? Which patients would be most at risk?

DEHP and DIDP are plasticisers widely used in plastic products such as shower curtains, garden hoses, IV bags, nasogastric feeding tubes and umbilical artery to make them more flexible. DEHP can be released to indoor air from these plastic materials and is present at very low levels in medical products, foods packaged in plastic, and fluids from plastic intravenous tubings if used extensively as in the case of dialysis. Therefore, DEHP is present everywhere in the environment because of the use of plastic substances in our daily life. However, this amount is usually not at level of concern. DEHP was illegally added into beverage by food manufacturers intending to be an emulsifying agent to improve the appearance and taste.

Exposure to DEHP has produced a range of adverse effects in experimental animals, but those of greatest concern involve effects on the development of testicles and the production of normal sperm in young animals. Fertility was reduced in male mice that were exposed to DEHP. The age at first exposure to DEHP appears to have a clear influence on the degree and permanence of testicular damage. Tubular structure and spermatogenesis are more affected by prepubertal acute exposure than by postpubertal acute exposure. When exposure ceases prior to sexual maturity, the effect of DEHP on reproductive performance does not appear to be permanent. It is possible that the effects observed in animals studies could occur in humans. However, there are no human studies to date that show such effects. The greatest concern would be for very young male infants who have prolonged exposure



to multiple devices containing DEHP.

For oral exposure, no cases of death in humans were located. Data shows that DEHP is very unlikely to cause acute harm in humans. Acute exposure to large oral doses of DEHP can cause GI distress. The International Agency for Research on Cancer (IARC) classified DEHP as possibly carcinogenic to humans but there is inadequate evidence of carcinogenicity in humans. Studies in rats and mice indicate that DEHP can cause liver tumors in these animals. Whether or not DEHP contributes to human kidney damage is unclear. Moreover, absorption and breakdown of DEHP in humans is different from those in rats or mice, so the effects seen in rats and mice may not occur in humans.

To assess the potential risk, we can compare the amount of DEHP that patient received to the Tolerable Intake (TI) value for DEHP. The TI value is the dose of a compound that is not expected to produce adverse effects in exposed patients. Exceeding the safety reference value occasionally is unlikely to cause significant health risk provided that the average intake does not continuously exceed the safety reference value. For harm minimisation, we could identify the group of patients who could be exposing to relatively high levels of DEHP, such as male neonates, and use devices made of alternative materials or those made of PVC that does not contain DEHP (non-collapsible infusion bottle) when appropriate. For instance, amiodarone, an antiarrhythmics agent, may leach out DEHP and other plasticiser if given through collapsible PVC containers. To reduce the level of exposure in male neonates who are at most risk, we may recommend using glass or non-PVC container that does not contain DEHP for male neonates.

In conclusion, the risk of plasticisers in terms of fertility and carcinogenicity appears to be confined to animal models, and evidence of human harm upon exposure to these chemicals is scanty. However, as pharmacists, we should be mindful of possible unnecessary exposure to plasticisers due to leaching when administering medications as intravenous infusions. Resources like Handbook of Injectable Drug provide good guidance in this remit.

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