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EDITORIAL

Highlight report the food additive dammar resin is a rat hepatocarcinogen

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Recently, Gi and colleagues from Osaka University in Japan published a 52-week chronic toxicity study and a 104-week carcinogenicity study of dammar resin in F344 rats (Gi et al. 2018). The authors demonstrated that hepatocellular adenomas and carcinomas were induced at 2% dietary concentrations of dammar resin, corresponding to 242 mg/kg b.w./day, while 0.5% (178 mg/kg b.w./day) was the no-observed-adverse-effect level (NOAEL).

The results of Gi and colleagues are of high relevance, since dammar resin is used as a food additive and flavoring substance in drinks, frozen desserts and in chewing gum (Gi et al. 2018; Cohen et al. 2017, USP 2012). It is produced as an exudate from trees of Agathis, Hopea or Shorea genera (Gi et al. 2018). For risk evaluation, it should be considered that the concentrations of dammar resin in food are orders of magnitude lower than the doses used in the present study (Gi et al. 2018). Moreover, dammar resin was negative in genotoxicity and mutagenicity tests, including chromosomal aberration tests and the mouse bone marrow micronucleus assay (Hayashi et al. 2000), suggesting that the compound acts as a non-genotoxic rat liver carcinogen. Therefore, studies are required to analyze whether dammar resin acts similarly in rat and human hepatocytes or there are major differences. In vitro cultures of primary hepatocytes represent a well-established tool for interspecies comparison (Vatakuti et al. 2017; Gu et al. 2018; Rodrigues et al. 2018; Arbo et al. 2016; Ghallab et al. 2016; Ghallab 2017a, b; Hammad 2013; Hammad et al. 2015). Readout comprises not only the cytotoxicity but also gene expression and hepatocellular functions (Deharde et al. 2016; Godoy et al. 2016, 2018; Jansen et al. 2017; Reif et al. 2015; Grinberg et al. 2014; Stöber 2016; Hammad et al. 2017, 2018). This is of interest, since dammar resin induces at least seven cytochrome P450 isoforms rodents in vivo and also generates reactive oxygen species in rat liver (Gi et al. 2018), key events known to be associated with non-genotoxic hepatocarcinogenesis (Cohen 2010; Hall et al. 2012; Leist et al. 2017; Godoy et al. 2013; Hewitt et al. 2007; Nwosu et al. 2017). Therefore, a comparison of these and similar endpoints, e.g. nuclear receptor activation, in rat and human hepatocytes will be an important step to improve the risk assessment of dammar resin as a food additive.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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