

## 4-Methylimidazole Risks on Our Life

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### Editorial

#### Introduction

Caramel colors of foods have been grouped in 4 classes by the Joint FAO/WHO (Food and Agriculture Organization of the United Nations/World Health Organization) Expert Committee on Food Additives (JECFA), and the European Union Scientific Committee for Food [1]. 4-Methylimidazole (4-MI) (a heterocyclic organic chemical compound) is subjected to unavoidable formation during cooking in some foods and beverages, including coffee, beers, soy sauces. Some of these soft drinks which use caramel coloring will contain 4-MEI [2]. 4-MEI (4-Methylimidazole) is light yellow, 4-MEI is used as a chemical intermediate in the manufacture of photographic chemicals, dyes and some pigments and some rubbers. 4-MEI is formed as a result of the interaction of ammonia with reducing sugars [1]. It will be used as byproduct in some foods and beverages during some of cooking process associated with heat and browning. For example cola drinks may contain more than 100 µg of this compound per 12 ounce serving [3,4].

The toxicity of 4-MEI has been reported in many International agencies including the National Toxicology Program [4] and many articles. In 2007, NTP reported "clear evidence of carcinogenic activity" of 4-MEI in animal studies, based on increased incidences of alveolar/bronchiolar neoplasms [5].

The National Toxicology Program (NTP) conducted a two year feeding cancer bioassay of 4-MEI in mice and rats. In F344/N rat's ambiguous evidence of carcinogenic activity in female rats based on incidences of mononuclear cell leukemia and no evidence of carcinogenic activity in male rats were observed [6]. Chromosome aberration (CA) assay is one of methods to measure cytotoxicity and genotoxicity [7]. In 2015, Tazehkand et al. [8] reported that 4-MEI might not anti-genotoxic and protective effects in bone marrow cells of Swiss Albino Mice, because 4-MEI could not reduce the chromosomal aberrations induced by EMS. In 2016, Tazehkand et al. [9] reported that 4-MEI induced structural CAs at all concentrations for 12 h and at highest concentration for 24 h treatment periods and decreased the MI at highest concentration for 12 h and at all concentrations for 24 h in bone marrow cells of Swiss Albino mice. This result showed that 4-MEI

has cytotoxic and genotoxic effect in bone marrow cells of Swiss Albino mice [9]. At another research from same researchers 4-MEI has cytotoxic effect on 3T3-L1 and colon cancer cell lines and has necrotic effect on rat liver cells [10,11].

MacKenzie et al. [12] observed that female and male rats given caramel color IV (110 mg 4MEI/kg body weight) in drinking water at concentration of 10 g/kg for 2 years had significantly lower body weights, but not observed any histopathological changes [12]. In another study, Bu et al. [13] reported that 4-MEI at lower concentrations ( $\leq 100$  µg/ml) has no significant effect on the biological characteristics, including proliferation, apoptosis, migration and genes of hematogenesis expression and differentiation of BMSCs. Therefore, relatively low concentration of 4-MI in foods and beverages may have no toxic effect on BMSCs [13].

Therefore, it can be concluded that 4-MEI might pose a potential risk for humans. However, it must be investigated in other test systems for genotoxic and cytotoxic effects.

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