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Review

Anthraquinones, the Dr Jekyll and Mr Hyde of the food pigment family

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A B S T R A C T

Anthraquinones constitute the largest group of quinoid pigments with about 700 compounds described. Their role as food colorants is strongly discussed in the industry and among scientists, due to the 9,10-anthracenedione structure, which is a good candidate for DNA interaction, with subsequent positive and/or negative effect(s). Benefits (Dr Jekyll) and inconveniences (Mr Hyde) of three anthraquinones from a plant (madder color), an insect (cochineal extract) and filamentous fungi (Arpink Red) are presented in this review. For example excellent stability in food formulation and variety of hues are opposed to allergenicity and carcinogenicity. All the anthraquinone molecules are not biologically active and research effort is requested for this strange group of food pigments.

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1. Introduction

Natural pigments and colorants used in food belong to diverse chemical groups, such as carotenoids, anthocyanins, chlorophylls, betalains, melanins, or flavins. The stability of these natural colorants is quite an issue because they are highly unsaturated compounds sensitive to light, heat, and oxygen. Carminic acid, carmine and cochineal extract are among the more stable food pigments and colorants. Their structures are based on the anthraquinone skeleton (Fig. 1). Among this largest group of pigments of quinoid nature (700 compounds), most of the anthraquinones of interest are derivatives of the basic structure 9,10-anthracenedione, tricyclic aromatic organic compounds with formula $C_{14}H_8O_2$. Hydroxyanthraquinoid (HAQN) usually refers to hydroxylated 9,10-anthracenedione (from mono-, di-, tri-, tetra-, up (theoretically) to octa-). HAQNs absorb visible light and are colored. Anthraquinones can be found in plants, insects, lichens and filamentous fungi (Caro et al., 2012; Gessler, Egorova, & Belozerskaya, 2013).

The present review summarizes the past and current uses of anthraquinone derivatives in the food industry, compares the benefits (Dr Jekyll) and the inconveniences (Mr Hyde) of three molecules, and gives exploration trends about new sources or production processes.

2. Case study #1: European madder root extract

The roots of the well-known plant madder *Rubia tinctorum* L. (family: Rubiaceae) (Fig. 2a) supply a number of coloring HAQN substances. Its pigments are present as glycosides and aglycones, up to 2–3.5% of dry weight. The color shades of madder vary from scarlet, carmine red, pink (high content of pseudopurpurin and/or purpurin, called pink madder or rose madder), to red with a bluish tint (alizarin lakes).

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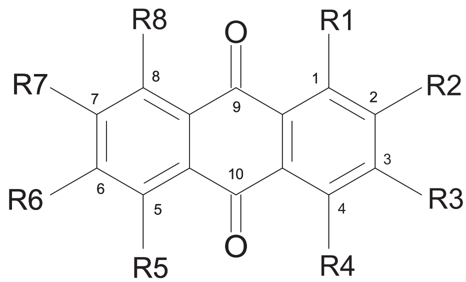

Fig. 1. Anthraquinone, general structure.

Madder color was long accepted for use as a food additive in Japan and South-Korea, but not in the United States of America (USA) and the European Union (EU). It was present among food additives that were already marketed or used on the date of the amendment of the Japanese Food Sanitation Law in 1995 and then appeared in the List of Existing Food Additives. As one of coloring agents, its use was limited to wakame, kelp, meat, fresh fishes and shellfish (including meat of whales), tea, beans, and vegetables. Production of madder root in Japan was 5 tons in 2002 and 3 tons in 2003 plus the unknown volume of imports (JFAEC, 2004).

There have been a number of genotoxicity studies on madder color and its constituents. From a "Dr Jekyll point of view" the presence of purpurin (1,2,4-trihydroxy-9,10-anthraquinone) in bacterial mutagenicity assays was found responsible for a marked inhibition of mutagenicity induced by food-derived heterocyclic amines (Marczylo et al., 1999). In another study, four anthraquinone pigments, among them alizarin and purpurin, showed significant antigenotoxic activities on DNA damage induced by carcinogens in *Drosophila* (Takahashi et al., 2001).

Ten years later, "the Mr Hyde effect" started to be confirmed as madder color was proven to exert carcinogenicity in the rat kidney and liver (Inoue, Yoshida, Takahashi, Fujimoto, et al., 2009; Inoue, Yoshida, Takahashi, Shibutani, et al., 2009).

The Japanese Ministry of Health, Labor and Welfare of Japan concluded that no ADI (Acceptable Dairy Intake) could be established for this substance, delisted madder color and prohibited its use in food (JFAEC, 2004).

3. Case study #2: carminic acid, carmine, cochineal extract

Carminic acid, carmine, and cochineal extract are produced in Peru, Bolivia, Mexico, Chile and Spain (Canary islands) from the dried bodies of female cochineal insects (*Dactylopius coccus*) (Fig. 2B), primarily grown on *Opuntia* cacti. The pigments can create red, orange, purple and pink shades depending on formulation.

These dyes are allowed by most of the food laws in different countries, such as the Food and Drug Administration (FDA) of the USA and the European Union where the food additive identification code is E120.

The chemical structure of carminic acid, the main pigment of cochineal, consists of a glucose unit which is attached to an anthraquinone (Fig. 3). Carminic acid is soluble in water, alcohol, acid and alkaline solutions. It presents good light stability and its color varies depending on pH. Because of its carbonyl and hydroxyl groups, carminic acid is ideally suited for coordination bonding with metals, creating carmine. Some cationic metal complexes can form lakes, giving precipitates of different colors (Borges, Tejera, Díaz, Esparza, & Ibáñez, 2012).

The coloring is currently used in a variety of products such as ice creams, yogurts, fruit drinks, candies, alcoholic drinks, and meat products (JFAEC, 2004).

While carmine is considered as a safe and effective natural alternative to synthetic red color FD&C Red #40, manufacturers have faced pressure from vegans, vegetarians, and shoppers seeking kosher and halal products to replace it, plus those suffering from the 'ick' factor (Watson, 2013a). This 'ick' factor is the main consumer issue for

Fig. 2. Sources of anthraquinone pigments. A. Madder root, *Rubia tinctorum* (plant); B. cochineal, *Dactylopius coccus* (insect); C. red colored filamentous fungi.

carminic acid, carmine and cochineal extract and it started when these colorings were implicated in adverse reactions, i.e. anaphylactic shock reaction in a small number of people due to impurities in the preparation but not due to the pigment itself. In 1998, it was reported that IgE-mediated allergy might be caused by the consumption of carmine, due to the presence of protein or protein-derived residues. In another case an anaphylactic reaction occurred in a 35-year-old woman after she ingested mixed-fruit yogurt colored with carmine. Acute allergic reactions after ingestion of orange beverage, strawberry milk and red colored cocktail, all containing carmine, were also mentioned (Acero