



61st JECFA - Chemical and Technical Assessment (CTA), 2003

CURCUMIN

Chemical and Technical Assessment (CTA)

First draft prepared by Ivan Stankovic

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1 Summary

At the 44th and 51st meetings of JECFA, reference was made to the requirement for the results of a reproductive toxicity study on a substance complying with the specification for curcumin. The Report of the 51st meeting of JECFA also asked for information on the need and technological justification for alternative solvents for use in the current manufacturing processes of curcumin. The Call for Data for the 61st JECFA has requested once again the results of a reproductive toxicity study on curcumin and, in addition, information on intake.

Curcumin is the product obtained by solvent extraction of turmeric i.e., the ground rhizomes of *Curcuma longa* L. (*Curcuma domestica* Valetton) and purification of the extract by crystallization.

Colouring principles are present to the extent of 3-5 percent in turmeric. The product consists essentially of colouring principles 1,7-bis-(4-hydroxy-3-methoxy-phenyl)-hepta-1,6-diene-3,5-dione (also known as curcumin) and its desmethoxy- and bis-desmethoxy-derivatives in varying proportions. Minor amounts of oils and resins naturally occurring in turmeric may be present. Functional use of curcumin as a food additive is a colour. Current JECFA specifications for curcumin were prepared at the 57th meeting of JECFA (2001) and published in FNP 52 Add. 9 (2001), superseding specifications prepared at the 55th meeting of JECFA (2000) and published in FNP 52 Add. 8 (2000).

The principal colouring components of curcumin exhibit a keto-enol tautomerism and antioxidative properties. Curcumin is an oil soluble pigment, practically insoluble in water at acidic and neutral pH, soluble in alkali. It is stable at high temperatures and in acids, but unstable in alkaline conditions and in the presence of light.

Note: In this document the use of the term curcumin refers specifically to material obtained by solvent extraction of turmeric, for which specifications have been developed.

2 Description

2.1 Nature of the product

Curcumin (synonyms: turmeric yellow, kurkum, INS No. 100(i)) is an orange-yellow crystalline powder. (FNP 52 add. 9, Merck Index, 2000, EC Directive 94/36/EC). Minor amounts of oils and resins naturally occurring in turmeric may be present.

2.2 Historical use

The origin of the plant *Curcuma longa* L., which belongs to Zingiberaceae family is India. The plant is distributed throughout tropical and subtropical regions of the world, being widely cultivated in southeast Asian countries. Turmeric, i.e., the ground rhizomes of *Curcuma longa* L., has a long history of use in food as a spice, mainly as an ingredient in many varieties of curry powders and sauces, where curcumin from turmeric is a main colouring substance.

2.3 Natural vs. synthetic origin

JECFA specifications define only curcumin extracted from natural source materials. It can also be produced by chemical synthesis (Lampe and Milobedzka, 1913, Pabon, 1964, Merck Inex). Synthetic curcumin is not used as a food additive.

3 Manufacturing

3.1 General

Turmeric is subjected to solvent extraction. The JECFA specifications monograph for Curcumin (FNP 52 Add. 9, 2001) lists acetone, methanol, ethanol, and isopropanol as suitable solvents. The European Commission Directive 95/45/EC lists the following solvents as suitable for the extraction: acetone, carbon dioxide, ethyl acetate, dichloromethane, n-butanol, methanol, ethanol, and hexane. Curcumin is recovered by crystallization from the extract. Minor amounts of oils and resins naturally occurring in turmeric may be present.

3.2 Detailed description

Curcumin is extracted from the dried root of the rhizome *Curcuma Longa*. The process of extraction requires the raw material to be ground into powder, and washed with a suitable solvent that selectively extracts colouring matter. This process after distillation of the solvent yields an oleoresin with colouring matter content in the region of 25-35 percent along with volatile oils and other resinous extractives. The oleoresin so obtained is subjected to further washes using selective solvents that can extract the curcumin pigment from the oleoresin. This process yields a powdered, purified food colour, known as curcumin powder, with over 90 percent colouring matter content and very little volatile oil and other dry matter of natural origin. The selection of solvents is done with care to meet extractability and regulatory criteria. The following solvents are considered suitable:

Isopropanol	In the curcumin manufacturing process isopropyl alcohol is used as a processing aid for purifying curcumin.
Ethyl acetate	With a restriction placed on the use of chlorinated solvents, such as dichloroethane, it is found that ethyl acetate, owing to its polarity, is a reasonable replacement providing acceptable quality of product and commercially viable yields.
Acetone	This is used as a solvent in the curcumin manufacturing process.
Carbon dioxide	This is not currently used in commercial production. However, it is listed in EC Directive 95/45/EC and has potential as a substitute for chlorinated solvents.
Methanol	This solvent is used occasionally as a processing aid for purification.
Ethanol	This solvent is used sparingly because curcumin is completely soluble in ethanol.
Hexane	

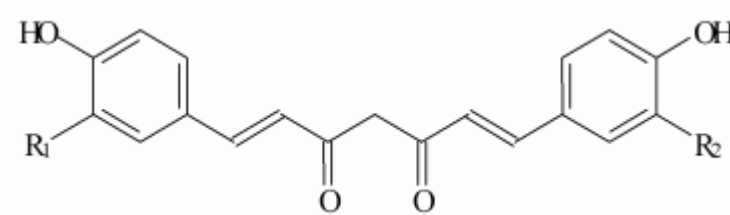
4 Chemical characterization

4.1 Composition of the food additive

The three principal colouring components of curcumin that are present in various proportions are all dicinnamoylmethane derivatives:

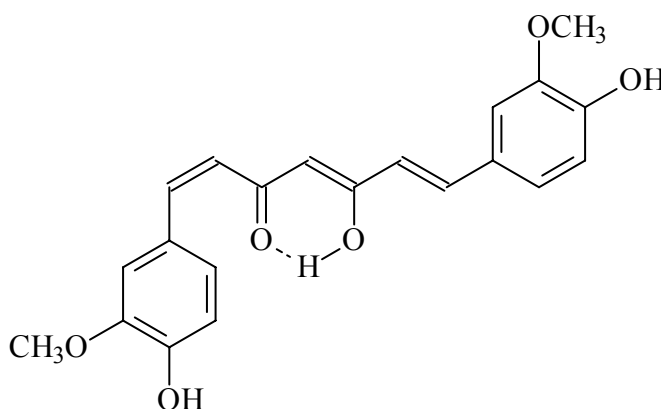
- 1) 1,7-Bis-(4-hydroxy-3-methoxyphenyl)-hepta-1,6-diene-3,5-dione
= diferuloylmethane
(Chemical formula: C₂₁H₂₀O₆; C.A.S. number: 458-37-7, Formula weight: 368)
- 2) 1-(4-Hydroxyphenyl)-7-(4-hydroxy-3-methoxyphenyl)-hepta-1,6-diene-3,5-dione
= p-hydroxycinnamoylferuloylmethane
(Chemical formula: C₂₀H₁₈O₅; C.A.S. number: 33171-16-3, Formula weight: 338)

- 3) 1,7-Bis-(4-hydroxyphenyl)-hepta-1,6-diene-3,5-dione
 = p,p-dihydroxydicinnamoylmethane
 (Chemical formula: C₁₉H₁₆O₄; C.A.S. number: 33171-05-0, Formula weight: 308)



- 1) R₁ = R₂ = OCH₃
- 2) R₁ = OCH₃, R₂ = H
- 3) R₁ = R₂ = H

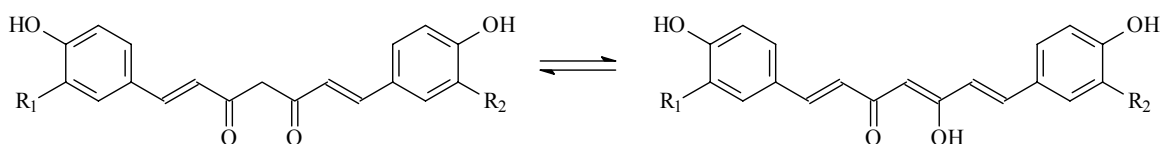
Besides these major constituents, three minor constituents can be isolated which are presumed to be the geometrical isomers of compounds 1-3, above. One of these is assumed to be the cis-trans geometrical isomer of compound 1 (which has the trans-trans configuration) based on its UV spectrum, lower melting point and lower stability in solutions and in the presence of light when compared to compound 1. (Srinivasan, 1952).



cis-trans geometrical isomer of Compound 1

Minor amounts of oils and resins naturally occurring in turmeric may be present in curcumin. The predominant constituents of these oils and resins appear to be sesquiterpene ketones and alcohols: α -turmeron, β -turmeron, curlon, zingiberen, ar-turmeron, turmenorol A, turmeronol B etc. (Ohshiro and Kuroyanagi, 1990, Imai and Morikiyo, 1990, Majeed, et al, 2000)

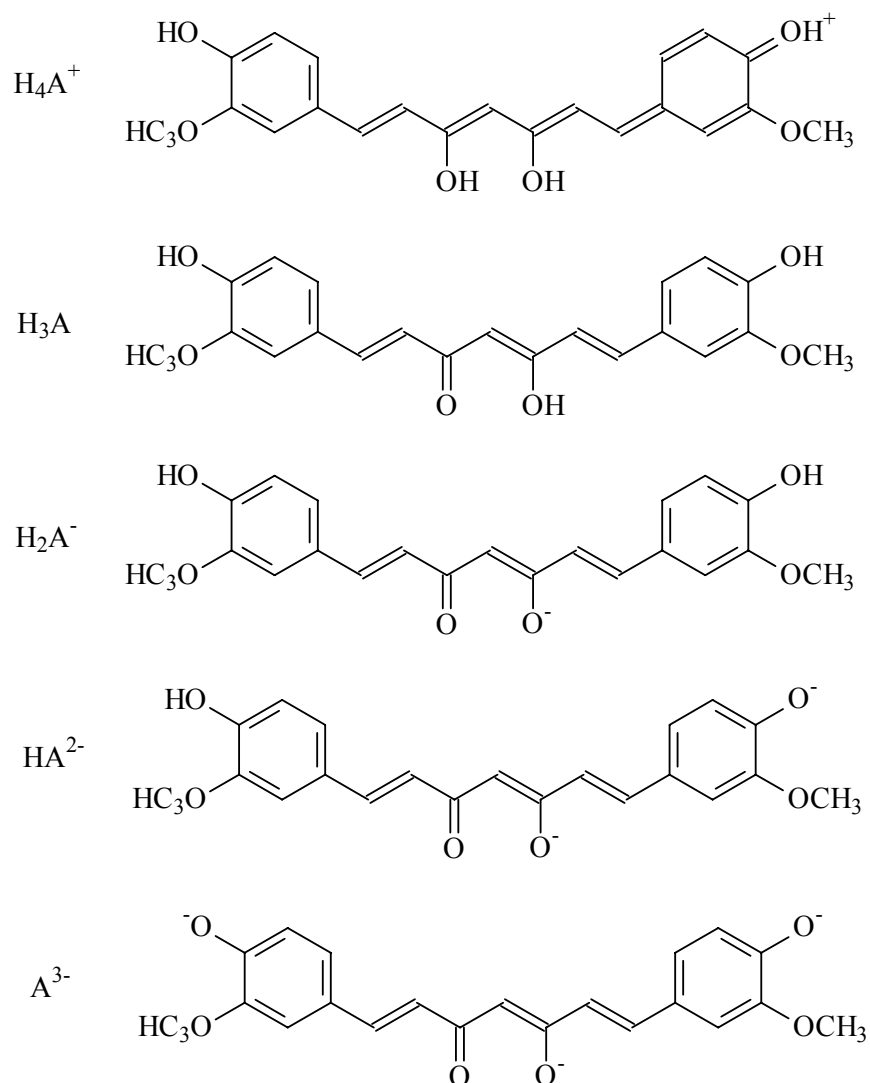
Compounds 1-3 exhibit keto-enol tautomerism:



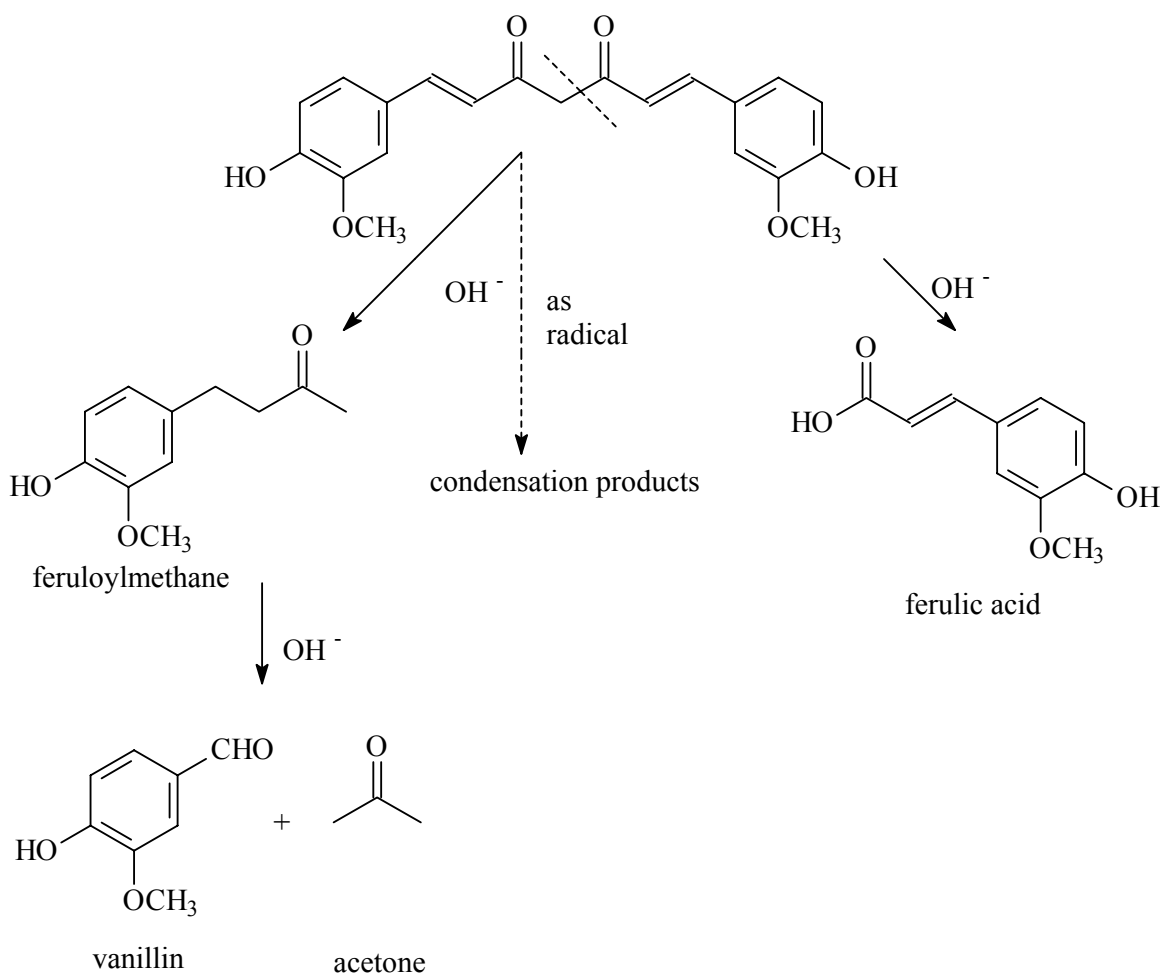
4.2 Physico-chemical properties

Curcumin is an oil-soluble pigment, practically insoluble in water at acidic and neutral pH, and soluble in alkali. Preparations of water-soluble curcumin by incorporation into various surfactant micellar systems (e.g. sodium dodecyl sulfate, cetylpyridinium bromide, gelatine, polysaccharides, polyethylenglycol, cyclodextrins) have been reported (Humphrey, 1980, Tonnesen, 2002). In solutions the principal colouring components of curcumin exhibit keto-enol tautomerism and, depending on the solvent, up to 95 percent are in the enol form.

The kinetics of hydrolytic degradative reactions of compound 1 (diferuloylmethane) over the pH range 1-11 was studied using HPLC technique (Tonnesen and Karlsen, 1985). At pH <1, aqueous solutions of diferuloylmethane have a red colour which indicates the protonated form (H₄A⁺). In the pH range 1-7, the majority of diferuloylmethane species are in the neutral form (H₃A). Water solubility is very low in this pH range and solutions are yellow. At pH >7.5, the colour changes to red. The pK_a values for the dissociation of the three acidic protons in compound 1 (forms H₂A⁻, HA²⁻ and A³⁻) have been determined to be 7.8, 8.5 and 9.0, respectively.



The principal colouring components of curcumin are relatively stable at acidic pH, but they rapidly decompose at pHs above neutral. In a study of alkaline degradation of compound 1 (Tonnesen and Karlsen, 1985a), products of decomposition at pH 7-10 were determined by HPLC. The initial degradation products are formed after 5 minutes and the chromatographic pattern obtained after 28 h at pH 8.5 is representative for alkaline degradation. Ferulic acid and feruloylmethane are formed initially. Feruloylmethane rapidly forms coloured (mostly yellow to brownish-yellow) condensation products. Degradation products formed by hydrolysis of feruloylmethane are vanillin and acetone and their amount increase with incubation time.



In another study (Wang et al, 1997) curcumin was incubated in 0.1 M phosphate buffer, pH 7.2 at 37°C, and about 90 percent was decomposed within 30 min. Trans-6-(4-hydroxy-3-methoxyphenyl)-2,4-dioxo-5-hexenal was predicted as major degradation product and vanillin, ferulic acid, feruloyl methane were identified as minor degradation products.

The authors of another study observed that compound 3 was less susceptible to degradation at pH 10.2 than compound 1 or compound 2 (Price and Buescher 1997).

In native form curcumin is not suitable as a colouring agent in aqueous solutions of pH > 7.

The principal colouring components of curcumin are not particularly stable to light, especially in solutions. After the photo-irradiation of compound 1, a cyclisation product was detected, as well as decomposition products, such as vanillic acid, vanillin, and ferulic acid (Sasaki et al, 1998). Commercial formulations of curcumin are available that are designed to minimize the inherent light instability.

4.3 Possible impurities (including degradation products)

Degradation products described previously, residual solvents and lead are the most important impurities. Residual solvents and the content of lead are limited according to JECFA specifications (FNP 52 add. 11).

4.4 Rationale for revision of specifications

JECFA is being asked to consider including ethyl acetate and carbon dioxide as alternative solvents in the JECFA specification monograph.

Ethyl acetate (ADI 0-25 mg/kg bw) has been evaluated by JECFA as a flavouring agent and as a carrier solvent (FNP 52 Add. 4). In the EU it is an approved solvent in the manufacture of curcumin (Directive 94/36/EC) with a maximum residue limit in curcumin of 50 mg/kg, singly or in combination with other approved solvents (Directive 95/45/EC). Ethyl acetate, due to its polarity, provides acceptable quality of

product and commercially viable yields. A residual limit of 50 mg/kg is appropriate for inclusion in the JECFA specification monograph.

Carbon dioxide, as a supercritical fluid, (ADI NS) is recognized by JECFA as an extraction solvent. It is also a carbonating agent, propellant, preservative and freezing agent. In the EU it is an approved solvent in the manufacture of curcumin (Directive 94/36/EC) although current information does not show that it is in use commercially. Because carbon dioxide is a gas no residual carbon dioxide will remain in the finished product, therefore a specification limit for residual carbon dioxide is not needed.

5 Functional uses

5.1 Technological function

The technological function of curcumin as a food additive is as a colour. It is insoluble in water, but water dispersible forms of turmeric extracts are available. Curcumin also has antioxidant properties.

5.2 Food categories and use levels

Curcumin is widely used to colour many foods. The Draft Codex General Standard for Food Additives provides an extensive list of such foods. Curcumin is listed for use in deary products, fats, oils and fat emulsions, edible ices, fruit and vegetable products, confectionery, cereal products, bakery wares, meat and meat products, fish and fish products, eggs and eggs products, spices, soups, sauces and protein products, foodstuffs intended for particular nutritional uses, beverages, ready-to-eat savouries and composite foods. Use levels of curcumin are in the range from 5 to 500 mg/kg depending on the food category.

6 Reactions and fate in food

Curcumin is stable in dry food. It is relatively stable to heat so it can be used in thermally treated foods.

Reported reactions of curcumin with food constituents are bleaching of colour by sulfur dioxide at levels in excess of 100 ppm and formation of complexes with some salts (citrate, phthalate). The principal colouring components of curcumin are apparently inert to chlorides, phosphates and bicarbonates (Tonnesen and Karlsen, 1985).

The principal colouring components of curcumin are effective antioxidants in food. The literature on the site of activity and the reaction mechanism(s) responsible for antioxidant effects are somewhat controversial, with most authors claiming that the antioxidant activity is due to the hydroxyl moiety (Sun, et al., 2002., Sreejayan and Rao, 1996, Barclay et al, 2000, Osawa et al, 1995, Venkatesan and Rao, 2000), while others invoke involvement of double bonds and carbonyl groups, separately or together, with para-hydroxy groups (Tonnesen and Greenhill, 1992, Sugiyama et al., 1996, Sreejayan and Rao, 1997). Studies showed that curcumin has a very powerful antioxidant effect (Sreejayan and Rao 1994, Osawa et al., 1995). Curcumin proved significantly more effective than other spices in its ability to prevent lipid peroxidation. Its antioxidant effect was eight times more powerful than vitamin E (Reddy and Lokesh, 1992) and it was significantly more effective in preventing lipid peroxide formation than the synthetic antioxidant BHT (Majeed et al., 2000).

The antioxidant property of curcumin can prevent rancidity of foods and provide foodstuffs containing less oxidized fat or free radicals. The powerful anti-oxidation property of curcumin has an important role in keeping curry for a long time without it turning rancid.

The principal colouring components of curcumin scavenge free radicals at the cost of becoming weak free radicals themselves. According to one research report (Majeed et al., 2000) these "second hand" free radicals are unreactive and short-lived products (unlike those of synthetic phenolics, e.g., BHT or BHA) and do not pose a health hazard.

It is reported that in organic solvents and in some micellar solubilized systems the principal colouring components of curcumin act as photo-sensitizers of singlet oxygen, superoxide and free radicals (Tonnesen et al., 1986, Chignell et al., 1994). This ability can have a destabilizing effect on curcumin-containing products. On the other hand, light-induced oxidation can be applied in systems with biological destructive behaviour; e.g. in the killing of bacteria (Tonnesen et al., 1987).

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