Majalah Farmasi Indonesia, 12(3), 115-119, 2001

CHEMICAL CONTENT OF TURMERIC ;CURCUMIN AND ITS DERIVATIVES
(KANDUNGAN KIMIA TURMERIK; KURKUMIN DAN TURUNANNYA)

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ABSTRACT

A brief review on turmeric from the stand-point of chemical content are presented. Recent studies on turmeric showed that at least 7 compounds of curcumin derivatives have been found, including cyclocurcumin the newer curcumin derivative.

Keywords : curcumin, curcumin derivatives.

ABSTRAK

Tulisan ini menyajikan tinjauan yang jelas tentang turmerik, dari sudut pandang kandungan kimianya. Penelitian terakhir pada turmerik, menunjukkan bahwa paling tidak 7 senyawa dari kurkumin dan turunannya telah ditemukan; termasuk siklokurkumin yang merupakan turunan kurkumin yang terbaru.

Kata kunci : kurkumin, turunan kurkumin.

Introduction

Curcuma longa L (Zingiberaceae) is a perennial herb widely cultivated in tropical regions of Asia. Its rhizoma is extensively used for imparting colour and flavour to food. In Europe it is known as *Indiana Saffron* and widely marketed as dry powder called turmeric. Turmeric is also used for medical purposes, thus turmeric mixed with slaked lime is known as household remedy for the treatment of sprains and swellings caused by injury. For this purpose it is applied locally over the affected area. Current traditional Asian medicine claims the use of turmeric against biliary disorders, anorexia, coryza, diabetic wounds, hepatic disorders, rheumatism and sinusitis, when translated into terms of modern medicine. The traditional medicine in China uses *Curcuma longa* in diseases which are assosiated with abdominal pains, and icterus (Ammon and Wahl, 1991).

Curcuma longa still occupies an important position as almost every food in India should contain it. Religius ceremonies always make use of turmeric in any form. The production of turmeric in Indonesia was estimated about 40.000 tons per year (Sudiarto and Effendi, 1991), while world wide it was about 160.000 tons per year in 1980 (Tonnesen, 1986). In Indonesia turmeric is known as a traditonal Indonesia spice mainly for its widely use as traditional-drugs so called " Jamu" and partly for its flavour. Different yellow pigments have been isolated from the rhizomes of *C. Longa* and related species (Kuroyanagi and Natori, 1970). These pigments were known as curcuminoids and curcumin was found to be the main constituents of those pigments.

Chemistry of Curcumin and its Derivatives.

Srinivasan (1953) has demonstrated the presence of three major constituents of which curcumin (diferuloylmethane) was the largest component, the two others being derivatives of curcumin *i.e.* demethoxy curcumin and bisdemethoxy curcumin. Curcumin was isolated in 1815 by Vogel and Pelletier and the chemical structure of curcumin as diferuloylmethane was determinated by Lampe in 1910 (Majeed *et al*, 1995).

Biosynthesis. The biosynthesis of curcumin in *Curcuma longa* was studied by Roughley and Whiting (1973). As diarylheptanoid, curcumin shows 3,5-bis oxygenation 1,2 and 6,7 unsaturation in the heptane chain. This pattern has provoked the very reasonable suggestion that biosynthesis of curcumin involves two ferulic units which are coupled to a central carbon provided by malonic acid (Fig. 1). The other suggestion of the biosynthesis of curcumin, is the condensation of one molecule ferulic acid with several malonic acid moieties, followed by cyclization, reduction and dehydration which lead to the curcumin molecule.

Fig. 1 Propose Biosynthesis of Curcumin

Synthesis. The pure compound curcumin is hardly to obtain. Isolation of pure curcumin from plant material is time consuming whereas pure natural curcumin is not produced commercially. Curcumin sold on the marked contains a mixtute of three naturally occuring curcuminoids, with curcumin as the main constituent even if labelled as "pure" (Tonnesen, 1986). Moreover, Majeed *et al* (1995) reported that curcuminiods consisted more than just three curcumin derivatives. Thus, to prepare the pure compound of curcumin, a synthesis method is the best way.

Curcumin can be prepared via a condensation reaction of 2,4-pentanedione with vanillin, although its synthesis requires some special reagents to avoid the straightforward aldol type condensation (Knoevenagel condensation) between the two starting materials. Since the central methylene-group of 2,4-pentanedione is more acidic than the methyl one in terminal position, the result would be a condensation of the central methylene-group of 2,4-pentanedione with vanillin yielding a substituted 3-benzylidene-2,4-pentanedione (Van der Goot, 1997). To avoid this reaction Pabon (1964) used the borium complex of 2,4-pentanedione for coupling with vanillin to afford the curcumin borium complex. After mild acidification the curcumin borium complex decomposes to curcumin it self.

Fig. 2. Structure of Curcuminoid **(1) β-diketone form (2) Keto-enol form**

A = Curcumin, $R_1 = R_2 = OCH_3$; 1,7- bis-(4-hydroxy-3-methoyphenyl)1,6-heptadiene-3,5-dione ; Diferuloylmethane

B = Demethoxy curcumin, $R_1 = H$; $R_2 = OCH_3$ C = Bisdemethoxy curcumin, $R_1 = R_2 = H$

Curcumin gave vanillic acid and ferulic acid on boiling with alkali, whose constitution had already been established. A characteristic isoxazole derivative was obtained when treated with hydroxylamine. On treatment with acetic anhydride curcumin formed the diacetyl derivative, and on hydrogenation a tetrahydro derivative was obtained. Based on these, the structure of curcumin was established as diferuloyl methane (Fig. 2) (Majeed *et al*, 1995).

Attempting to synthesize curcumin by condensation of acetylacetone with vanilic aldehyde in the presence of ethanolic hydrogen chloride, Heller in 1914 obtained two products which differed from curcumin in their failure to react with boric acid and ferric chloride. They were called a and b curcumins. As 1,3-diketones form stable metalic complexes by reaction with ferric chloride, Heller concluded that normal curcumin, which give a deep reddish brown color with ferric chloride, has the keto-enol structure (Fig. 2. A.2), while the two isomers, which gave only a pale yellowish brown colour, have diketone structures, a and b being steroisomers of curcumin (Majeed *et al*, 1995). The two steroisomers of a and b curcumins might be a *trans-trans* curcumin (a form), and a *cic-cis* one (b form) (Fig. 3).

Fig. 3. The two Stereo Isomers of curcumin Synthesized by Heller (1914)
An (a) form : *trans-trans* Curcumin; (b) form : *cis-cis* Curcumin

Fig. 4. *Cis-trans* Geometrical Isomer of Curcumin

Beside these major consituents, a minor constituent is also isolated which was supposed to be the geometrical isomer of curcumin (Srinivasan, 1953). It was assumed to be *cis-trans* geometrical isomer of curcumin (Fig. 4) based on its UV spectrum, lower melting point and lower stability compared to curcumin which has a *trans-trans* configuration.

Recently in 1993, a new curcuminoid, cyclocurcumin was isolated from the nematocidally active fraction of turmeric, together with other known curcuminoids, curcumin, demethoxy curcumin and bisdemethoxy curcumin. These three known curcuminoids did not show any nematocidal activity (Majeed *et al*, 1995).

Cyclocurcumin was isolated from the mother liquor by repeated purification, as a yellow gum. From its molecular formula (which was same as curcumin), ^{1}H-NMR, UV, ^{13}C-NMR, ^{13}C-^{1}H-COSY spectroscopic studies it was concluded that the structure of cyclocurcumin is as shown in Fig. 5. This derivative may be formed from curcumin by an intramolecular Michael addition of the enol oxygen to the enone group (Majeed *et al*, 1995). This route was confirmed by acid catalysed cyclisation of curcumin to cyclocurcumin. Since cyclocurcumin isolated from turmeric is racemic, it was first thought to be an artifact from curcumin during isolation, but high performance liquid chromatography (HPLC) analysis revealed that cyclocurcumin exists in the chloroform extract from the beginning and could actually be isolated from the chloroform extract in 0,8% yield.

Fig. 5. Structure of Cyclocurcumin

The last steps in the biosynthesys of cyclocurcumin could be as follows (Supardjan, 1999)

Fig. 6. Propose Biosynthesis of Cyclocurcumin

As may be seen in the structure of cyclocurcumin, the C-2 of the 2,3-dihydropyranone system forms a chiral carbon, and the cyclocurcumin is present as racemic mixture.

Fig. 7. The Racemic form of Cyclocurcumin

Interestingly, cyclocurcumin did not show nematocidal activity, but when the four curcuminoids were mixed, a strong nematocidal activity appeared; so it was concluded that the strong nematocidal activity of turmeric is due to a synergistic action of the curcuminoids.

This example shows a synergistic action of the plural constituents is important for understanding the biological effect of crude drugs as traditional medicines and species (Majeed *et al*, 1995).

Resume

Recent studies on turmeric showed that at least seven compounds have been found, that is : curcumin, demethoxy curcumin and bisdemethoxy curcumin (as mayor constituents) ; *trans-trans* curcumin ; *cis-cis* curcumin; *cis-trans* curcumin and cyclocurcumin as racemic mixture (as minor constituents).

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