



Selected Patents On Food Dye: Curcuma Longa

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Abstract:

- Background: Traditionally, turmeric has been used for a long time. Later, active constituents were separated, and some patents were filed for the techniques and formulations related to curcumin.
- Objective: The main aim of the review is to compile data related to curcumin or turmeric from various patents.
- Methods: Literature survey is done to exploit the patents using various survey engines like google patents, google scholar, science direct, etc.
- Results: This review comprises the patents related to curcumin, which have been granted so far. In these patents, there are different formulations of curcumin, i.e., complexes of curcumin, water-soluble curcumin complexes, curcumin metal color complexes, etc., which are meant to improve its aqueous solubility and bioavailability
- Conclusion: New pharmacological applications of the drug are also reported in some patents. The synthesis of various formulations with a combination of curcumin is also discussed. Some patents are also discussed, the improvement in various physicochemical properties with different techniques or formulations.

Keywords: curcumin, turmeric, patents, curcuma longa, curcuma domestica

Introduction

Curcuma domestica or *Curcuma longa* are botanical names of turmeric, a topical herb belonging to the family Zingiberaceae(1). It is found in Southern Asia. In Asian countries, the yellow powder extracted from its natural rhizomes has been used as a vegetable dye, yellow in color(2). In foods, it is used as a spice, an essential constituent of curry powder. It is a folk medicine for various disorders like inflammation, skin cancer, and GIT disorders like inflammatory bowel diseases. Turmeric comprises three coloring pigments, which have a robust lipophilic nature. These are collectively known as curcuminoids. These are curcumin diferuloylmethane, demethoxycurcumin hydroxycinnamoyl feruloyl methane, and bis-des- methoxycurcumin dihydroxydicinnamoyl methane. The essential oils of *curcumin domestica* and *curcumin xanthorrhiza* are extracted by steam distillation of dried rhizomes. D-Camphor 1%, Cyclo-isoprenemyr- cene 85%, and P-Tolylmethylcarbinol 5% are the main components of the essential oil(3).

Curcumin 1,7-bis(4-hydroxy-3-methoxyphenyl)-1,6-heptadien-3,5-dione is a derivative of polyphenol, which is hydrophobic and an antioxidant derived from turmeric. The main constituents of curcumin are 77% of diferuloylmethane, 17% of demethoxycurcumin, and 6% of bisdemethoxycurcumin(4). The ongoing research proves that curcumin shows potent anti-inflammatory, immunomodulatory, antiproliferative, and anticarcinogenic properties(5). It also protects cells and various tissues from different injury mechanisms. According to additional preclinical studies, it has been shown that curcumin is a promising therapeutic agent for multiple diseases and specific clinical conditions, e.g., cancer treatment, leukemia treatment, myocardial infarction, sepsis, radiation injury, etc.(6). Various molecular targets of curcumin have been identified and with these targets, interactions of curcumin was explained in various animal disease models. After that, curcumin was considered safe in animal models, and phase I clinical trials was done on higher doses(7).

The main problems associated with curcumin are its low bioavailability, low solubility and photodegradation, and poor stability at alkaline pH (8). When curcumin is given orally, a minimal amount can reach the tissues and blood. This low bioavailability is the limiting factor for its clinical use in preventing and treating proposed



diseases (9). Very low aqueous solubility is the primary reason for curcumin's low bioavailability, and its metabolism is rapid in the intestine, especially in human subjects. Poor aqueous solubility has hindered the development of pharmaceutical formulations for intravenous administration.

The extraction of natural curcumin is a pretty complex and costly process. There is no way to obtain a practically effective separation of curcumin itself from two demethoxyrelated compounds, along with which it is found in nature. Various attempts have been made to solve this problem. The most successful effort among these is the aldol condensations of vanillin 3-methoxy-4-hydroxybenzaldehyde and 24-pentanedione. The yield from this condensation is low.

The present study compiles data from various patents related to curcumin, comprising its use in the form of modified formulations to overcome its limitations to treat multiple diseases like inflammation, cancer, viral infections, etc., in the form of different drug delivery systems. Some attempts to achieve this target involve synthesizing its derivatives or complexes with a hydrophilic carrier. This review also summarises some landmarks in the research on the whole turmeric rhizome and its isolated active constituents to overcome the obstructions in exploiting its potential benefits.

Details of some selected patents on curcumin:

U.S. Patent Application No. 20060067998: To overcome the low absorption of oral curcumin, U.S. Published Patent Application No. 20060067998 revealed a drug delivery system, colloidal, for the parenteral administration of curcumin. Liposomal drug delivery systems, polymer-based nanoparticles, and microparticles were disclosed by the inventors (10).

W.O. 2009/144220 A1: This invention concerns the medical field, and it discovered the formulation of curcumin- cyclodextrin complex having pharmacological activities, particularly anti-tumor and anti-inflammatory. This invention is related to the compounds and methods for treating proliferative or inflammatory disorders. It revealed curcumin compositions that are water soluble and stable. The water-soluble compounds of curcumin preferred were the cyclodextrin complexes and their stereoisomers. The molecule was converted into its acylated and glycosylated derivatives to prepare the water-soluble curcumin compound. Lyophilization of these water-soluble curcumin compounds could be done. According to this invention, these water-soluble curcumin compounds may be cyclodextrin derivatives of curcumin itself, most probably the beta or gamma-cyclodextrin complexes of curcumin.

The information related to the pharmaceutical compositions, which are therapeutically effective, is provided by this invention—the therapeutically active amount lies between 0,01 mg and 1000 mg per kilogram of body weight.

The inventors also highlight water-soluble curcumin compounds, e.g., medicament for treating proliferative disorders such as neoplasm, abnormal cell growth, malignant tumor, cancer, etc.(11).

W.O. 2009/023357 A2:The purpose of this invention was to describe the use of curcumin derivatives as radioprotectors, i.e., that provide resistance against radiation damage in a particular subject after administering a recommended dose of that agent to it. The agent may be a derivative or a metabolite of curcumin. The recommended dose of this agent was given to subjects after radiation exposure.

Further, information about the compositions and their synthesis methods that could act as radioprotectors was revealed. Some modifications were done to curcumin compounds, which were prepared in such a manner that they had antioxidant properties. These compounds were proven effective as radioprotectors to the G.I. tract and other tissues(12).

W.O. 2017/097805 A1: In this invention, curcumin and resveratrol were combined with decreasing chronic cerebral inflammation. In our brain, microglia cells are mainly responsible for inflammatory responses. This combination is also helpful in reducing chronic pain in the brain and the spinal cord. This synergistic effect on microglia may also be useful in controlling and preventing chronic inflammation associated with low-grade fevers, diabetes, obesity and athletic exertion, etc.(13).

US10159654B2: In this patent, the information for a formulation of curcuminoids with turmeric essential oils for enhancing its bioavailability was disclosed. Curcuminoids have curcumin as the main constituent, and Ar-



turmerone is the essential oil that can be obtained from turmeric. For effective oral drug delivery of curcumin, bioavailability should be enhanced, and this can be made possible by adding the essential oil of turmeric to curcuminoids (14).

US 7,763,289 B2: In this patent, a neutral composition was disclosed, consisting of a therapeutically active turmeric extract that acts as a neutralizing agent. The quantity of turmeric extract is about 0.05% to 10%, ratios with the essential oil are about 1:1 to 1:20, and the pH value of neutral composition lies between 2 to 5. In the invention, a skin care product is revealed in the form of lotion, which is non-staining in nature with a pH value of 1.5 to 7.0. Neutralizing agents may be extracted from the berries like blue or coffee, cherries, etc. It also contains an acidic solution like lemon juice, orange juice, acetic acid, etc.

This invention formulated a skincare product composed of turmeric and other components. The product did not show any stains on the skin after application. This product may be used in cosmetics for protective action and healing purposes. (15).

US 4,263,333: In this invention, a water-soluble metal- curcumin complex- was formed to produce various colors for foodstuff use. It is exploited to produce broadspectrum yellow blooms, which are suitable for foodstuffs. Metal curcumin complex showed stability towards light and heat¹⁶. Table 1 summarizes some of the patents granted about curcumin.

Table 1 List of some patents related to curcumin.

S. No.	Patent No.	Title	Techniques/ Formulation	Publication Date	Applicants	Inventors	Reference
1	US 4263333	Curcumin-metal color complexes	Complexation	21.04.1981	General Foods Corporation, White Plains, N.Y.	Il Y. Maing, New City; Irene Miller, New York, both of N.Y.	(16)
2	EP 0440885 B1	Combinations of compounds isolated from Curcuma SPP as anti-inflammatory agents.	Curcuma SPP as anti-inflammatory agents	06.04.94	PT DARIA-VARIA LABORATORIA JKuningan Barat No. 26 Jakarta 12710ID	Oel Ban Liang JalanSumur Bandung 6 BandungID	(17)
3	US 5679864	Process for the synthesis of curcumin-related compounds	-	21.10.1997	Gene Print Inc., BalaCynwyd, Pa.	Mark Harry Krackov. West Chester, Pa.; Harold Edward Bellis, Wilmington, Del.	(18)
4	US 5897865	Turmeric for skin treating disorders	-	27.04.1999	-	Van Bich Nguyen, 927 Eastham Ct., 24, Crofton, Md. 21114	(19)
5	AU 0600482 0.4	Phospholipid complexes of curcumin having improved	Complexation	13.09.2007	IndenaS.p.A.	Giori, Andrea;Franceschi, Federico	(20)



		bioavailability					
6	U.S. 2008/01 38400 A1	Liposomal curcumin treatment diseases for of	Liposomes	12.06.2 008	Board Of Regents, The University Of Texas System, Austin, Tx US	RAZELLE KURZROCK , Bellaire, TX US; LAN LI, HOUSTON, TX US; KAPIL MEHTA, Bellaire, TX US; BHARAT BHUSHAN AGGARAW AL, HOUSTON, TX US; LAWRENC E HELSON, 7Quakertown , PA US	(21)
7	U.S. 2009/00 04334 A1	Dietary nutritional supplements for healthcare	-	01.01.2 009	-	Vijaya Nair, Bedford, NY U.S.	(22)
8	U.S. 2009/00 47371 A1	Pharmaceutical composition comprising curcumin and resveratrol and uses thereof in medical field	-	19.02.2 009	Safinvestm ent Holding Ag	DamianoTuri ni, Firenze IT, Stefan Coccoloni, Firenze IT	(23)
9	WO 2009/14 4220 A1	Water soluble curcumin compositions for use in anti-cancer and anti- inflammatory therapy	Anti-cancer and anti-inflammatory compositions	03.12.2 009	UNIVERS ITE LIBRE DE BRUXELL ES BE/BE; Avenue F.D. Roosevelt 50 CP1 61, B-1050 Bruxelles BE. UNI- VERSITE DE LIEGE BE/BE; Place du 20 août, B- 4000 Liege BE.	NEVEN, Philippe BE/BE; Rue des Martyrs 47, B-4550 Nandrin BE. SERTEYN, Didier BE/BE; Baugnee 13 B, B-4163 Tavier BE. DELARGE DECEASED, Jacques.KIS S, Robert BE/BE; Consciencst raat 34 H, Bus 3, B- 1600 St PietersLeeuw BE. MATHIEU, Veronique BE/BE; Av.	(35)



						Des Camelias 6, B-1 150 Brussels BE.CATAL DO, Didier BE/BE; Chemin du Vieux Puits, 4, B-4877 Olne BE. ROCKS, Natacha BE/BE; Route de Liege 182, B-4720 La Calamine BE.	
10	WO 2009/02 3357 A2	Curcumin derivatives and their use as radioprotectors	Radioprotectors	19.02.2 009	UNIVERS ITY OF ROCHEST ER US/US; 601 Elmwood PAvenue, Box Ott/oca, Rochester, NY 14642 US.	OKUNIEFF, Paul US/US; 14 Park Place, Rochester, NY 14625 US. ZHANG, LurongUS/U. S.; 62 Lattimore Road, Rochester, NY 14620 US. LIU, Chaomei US/US; 171 Rossiter Road, #1, Rochester, NY 14620 US. SUN, Weimin US/US; 171 Rossiter Road, #2, Rochester, NY	(12)
12	US 7763289 B2	Topical turmeric skin care products	Skin care products	27/07/2 010	JoAl's Products, LLC, Saginaw, MI US	Alexander A. Bommarito, Freeland, MI US	(15)
13	U.S. 2010/01 79103 A1	Curcumin cyclodex trin combination for preventing or treating various diseases	-	15.07.2 010	-	Ketan Desai, Easton, PA US	(24)
14	U.S.	Selective	Anti-diabetic	23.09.2	The	Drew	(25)



	2010/02 40581 A1	proteasome inhibitors For treating diabetes	formulation	010	Trustees of Columbia University in the City of New York, New York, NY US	Tortoriello, Jersey City, NJ U.S.: Stuart PWeisberg, New York, NY U.S.	
15	US 7879373 B2	Composition to enhance the bioavailability of curcumin	-	01.02.2 011	Arjuna Natural Extracis, Ltd., Alwaye IN	Benny Antony, Ankamaly IN	(26)
16	U.S. 2011/01 90399 A1	Curcumin nanoparticles and methods of producing the same	Nanoparticles	04.08.2 011	Santosh Kumar Kar, New Delhi IN	Santosh Kumar Kar, New Delhi IN; Feroz Akhtar, New Delhi IN; Gopesh Ray, New Delhi IN; Atul Kumar Pandey, New Delhi IN	(27)
17	W.O. 2012/03 5480 A2	Pharmaceutical compositions of curcumin	liquid pharmaceutical compositions	22.03.2 012	Cadila Pharmaceu ticals Limited IN/IN; Cadila Corporate Campus, Sarkhej - Dholka Road, Bhat, Ahmedaba d 382210 IN.	KHAMAR, Bakulesh Mafatlal GOGIA, Ashish Premkumar GODA, Chirag Chand rakant SHENOY, Dinesh Balkunje SHRIVAST AVA, Rajneesh Ramesh PATRAVAL E, Vandana MODI, Indravadan Ambalal LADDHA, Ritu Nitin KHAN, Imran	(28)



						Ahmad Cadila Pharmaceuticals Limited, Cadila Corporate Campus Sarkhej - Dholka Road, Bhat, Ahmedabad 0, 38221, IN	
18	U.S. 2012/01 95949 A1	Turmeric pigment composition and method for preparing same	Colouring agent	02.08.2 012	SAN-E GEN F.F.I., INC., Toyonaka-shi JP	Takeshi Miuchi, Toyonaka-shi JP; Masayuki Nishino, Toyonaka-shi JP; Yasushi Sasaki, Toyonaka-shi JP; Takashi Morimoto, Toyonaka-shi JP; Yoshiharu Tanaka, Toyonaka-shi JP	(29)
19	CA 2820845	A water soluble composition comprising curcumin having enhanced bioavailability and process thereof	-	22.11.2 012	Omniactive Health Technologies Ltd. IN	Deshpande, Jayant Venkatesh, IN; Kulkarni, Shrinivas Krishna Rao, IN	(30)
20	US 8487139 B2	Curcumin and tetrahydrocurcumin derivatives	Curcumin and tetrahydrocurcumin derivatives	16.07.2 013	-	Krishnaswami Raja, Staten Island, NY US; Probal Banerjee, Staten Island, NY U.S.; Andrew Auerbach, Livingston, NJ U.S.; Wei Shi, Staten Island, NY U.S.; William L'Amoreaux, Freehold, NJ U.S.	(31)
21	W.O. 2013/17 6555 A1	Improved complexes and compositions containing curcumin	Complexation	28.11.2 013	CAVE, Harold Gordon NZ/NZ; c/- Level 12.	CAVE, Harold Gordon NZ/NZ; c/- Level 12.	(32)



					KPMG Centre, 85 Alexandra Street, Private Bag 3140, Hamilton, 3204 NZ.	KPMG Centre, 85 Alexandra Street, Private Bag 3140, Hamilton, 3204 NZ.	
22	U.S. 2014/01 63116 A1	Method of treating cancer using a curcumindervative	Anti cancer formulation	12.06.2 014	DePuySynt hes Products, LLC, Raynham, MA US	Thomas M. DiMauro, Southboro, MA US	(33)
23	EP 2 249 852 B1	Soluble complexes of curcumin	Soluble complexes of curcumin	24.12.2 014	Novobion Oy 02160 Espoo FI	Parkkinen, Jaakko FI- 02160 Espoo FI	(34)
24	WO 2015/02 5263 A1	A novel composition of curcumin with enhanced bioavailability	-	26.02.2 015	Plant Lipids Private Limited IN/IN; Kolenchery , Cochin 6823 11 IN.	GOPI, Sreeraj; Kolenchery, Cochin 68231 1 IN.	(35)
25	US 8993013 B2	Composition to enhance the boavailability of curcumin	-	31.03.2 015	Arjuna Natural Extracts, Ltd., Alwaye IN	Benny Antony, Ankamaly IN	(36)
26	US 9012411 B2	Formulations from derivatives of curcumin, paclitaxel, and aspirin	Anti-inflammatory, analgesic and/or anti-cancer formulation	21.04.2 015	Organome d Corporatio n, Coventry, RI US	James N. Jacob, Saunderstow n, RI US	(37)
27	US 2016/00 39734 A1	Therapeutic curcumin derivatives	Therapeutic curcumin derivatives	11.02.2 016	STC.UNM , Albuquerq ue, NM US	David L. Vander Jagt, Albuquerque, NM US; Lorraine M. DECK, Albuquerque, NM US; Steve F. ABCOUWE R, Chelsea, MI US; Robert A. ORLANDO, Placitas, NM US; Robert E. ROYER, Albuquerque, NM US;	(38)



						Waylon M. WEBER, Albuquerque, NM US; Ekaterina V. BOBROVNIKOVA-MARJON, Sharon, MA US; Lucy A. HUNSAKER, Albuquerque, NM US	
28	U.S. 2017/0042835 A1	Pharmaceutical compositions comprising hemp and turmeric to treat pain and inflammation	-	16.02.2017	MewaSINGH, Zachary, LA US	MewaSINGH, Zachary, LA US	(39)
29	W.O. 2017/097805 A1	Curcumin and resveratrol for chronic inflammation	Antiinflammation	15.06.2017	DSM IP ASSETS B.V. NL/NL; Het Overloon 1, 641 1 TE Heerlen NL.	BUTT, Christopher Michael; c/o DSM Nutritional Products Ltd, Patent Department Wurmisweg 576, 4303 Kaiseraugst CH. RIEGGER, Christoph; c/o DSM Nutritional Products Ltd, Patent Department Wurmisweg 576, 4303 Kaiseraugst CH. WYNALDA, Kelly; c/o DSM Nutritional Products Ltd, Patent Department Wurmisweg 576, 4303 Kaiseraugst CH.	(40)
30	US 10159654 B2	Formulation of curcumin with enhanced	-	25/12/2018	Arjuna Natural Extracts,	Benny Antony, AnkamalyIN	(41)



		bioavailability of curcumin and method of preparation and treatment thereof			Ltd, Alwaye In		
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Conclusion:

The medicinal status of turmeric and its active constituents, curcuminoids, has been controversial since the beginning. *Ayurveda* claims it to be helpful in rheumatoid arthritis, inflammation, cancer, etc. Many ayurvedic formulations containing turmeric in one form or another are being used to treat their ailments from the beginning.

The ongoing preclinical research on this molecule has proved beneficial in arthritis, cancer, inflammation, immunomodulation, eczema, etc. It is also claimed to be an immunity booster in the COVID-19 pandemic era (42, 43). Still, medico personnel is not exploiting its medicinal benefits, preferably due to its low aqueous solubility, low and variable bioavailability, and degradability at alkaline pH. Resultingly its use is restricted to food supplements and cosmetic preparations only (44). Surprisingly, despite many beneficial therapeutic claims, curcumin is not being used in modern medicines alone or in combination.

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AUTHORS CONTRIBUTION: SA collected data from different sources. VB analysed the data and interpretation is done by MC. All manuscript is read and analysed by all authors.

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Graphical abstract:

