An Overview on Multipurpose Medicine: Turmeric (Haldi)

Shraddha Upadhye [1], Gitanjali Kasar [2], Lad S.D. [3], Kshirsagar M.B. [4], Rasve V.R. [5]

[1, 2, 3, 4] Students, [5] Assistant Professor,
Shri Amolak Jain Vidya Prasarak Mandal's College of Pharmaceutical Science and Research Center, Kada, Beed, Maharashtra, India.

Published in IJIRMPS (E-ISSN: 2349-7300), Volume 11, Issue 3 (May-June 2023)

Abstract
Curcumin, the major constituent of Curcuma longa L. (Zingiberaceae family) or turmeric, commonly used for cooking in Asian cuisine, is known to possess a broad range of pharmacological properties at relatively nontoxic doses. Curcumin is found to be effective against Staphylococcus aureus (S. aureus). As demonstrated by in vitro experiments, curcumin exerts even more potent effects when used in combination with various other antibacterial agents. Hence, curcumin which is a natural product derived from plant is believed to have profound medicinal benefits and could be potentially developed into a naturally derived antibiotic in the future. However, there are several noteworthy challenges in the development of curcumin as a medicine. S. aureus infections, particularly those caused by the multidrug-resistant strains, have emerged as a global health issue and urgent action is needed. It focuses on the antibacterial activities of curcumin against both methicillin-sensitive S. aureus (MSSA) and methicillin-resistant S. aureus (MRSA). We also attempt to highlight the potential challenges in the effort of developing curcumin into a therapeutic antibacterial agent. Antibiotic resistant bacteria are becoming an increasing threat worldwide, particularly in the healthcare setting. This has led researchers and healthcare providers to begin looking elsewhere for solutions. Curcumin, a phenolic compound from the spice turmeric, has antibacterial properties that may be able to treat potentially life-threatening hospital infections, such as those caused by Staphylococcus aureus and Pseudomonas aeruginosa. Turmeric has been used in Asian medicine for thousands of years as a general antimicrobial.

Keywords: Curcumin, Staphylococcus Aureus, Curcuma Longa, Pseudomonas Aerugiona

1. Introduction of Turmeric

Turmeric is a plant that has a very long history of medicinal use, dating back nearly 4000 years. In South-east Asia, turmeric is used not only as a principal spice but also as a component in religious ceremonies. Because of its brilliant yellow colour, turmeric is also known as “Indian saffron”. Modern medicine has begun to recognize its importance, as indicated by the over 3000 publications dealing with turmeric that came out within the last 25 years. This review first discusses in vitro

studies with turmeric, followed by animal studies, and finally studies carried out on humans; the safety and efficacy of turmeric are further addressed.

Figure 1: Turmeric

Turmeric, a plant in the ginger family, is native to South-east Asia and is grown commercially in that region, primarily in India. Its rhizome (underground stem) is used as a culinary spice and traditional medicine. Historically, turmeric was used in Ayurveda and other traditional Indian medical systems, as well as Eastern Asian medical systems such as traditional Chinese medicine. In India, it was traditionally used for disorders of the skin, upper respiratory tract, joints, and digestive system. Today, turmeric is promoted as a dietary supplement for a variety of conditions, including arthritis, digestive disorders, respiratory infections, allergies, liver disease, depression, and many others. Turmeric is a common spice and a major ingredient in curry powder. Curcumin is a major component of turmeric, and the activities of turmeric are commonly attributed to curcuminoids (curcumin and closely related substances). Curcumin gives turmeric its yellow color. Turmeric dietary supplements are made from the dried rhizome and typically contain a mixture of curcuminoids. Turmeric is also made into a paste for skin conditions.

1.1. Synonyms

Indian Saffron, Haldi (Hindi), Curcuma, Rhizomacur-cumac

1.2. Biological Source

Curcumin is the main active ingredient of turmeric, a spice obtained by grinding the dried rhizomes of the plant Curcuma longa turmeric dry rhizome is composed mainly of starch, having also carbohydrates, proteins, lipids, fiber, curcuminoids pigments, sesquiterpenes (turmerone, atlantone, zingiberone, turmeronol, germacrone, ucurcumene, B-sesquiphellanderene, bisacurone, curcumenone, dehydrocurdione, procurcumadiol, bis-acumol, curcumenols, zedoaronediol, bisabolene, and curlone), and caffeic acid. The curcuminoid content typically varies between 2% and 9%. Curcumin is the most abundant curcuminoid in turmeric, but traces of its precursors, desmethoxy curcumin and bisdemethoxy curcumin are also present.

2. Chemical Constituents

Turmeric contains about 5% flexible oil, amber, large amount of zingiberaceous starch and yellow substances known as curcuminoids. The main component of curcuminoids is known as curcumin (50-60%). Chemically, the Curcuma varieties contain hot oils, starch and curcumin. Curcumin and other related curcuminoids such as Demethoxy curcumin and Bisdemethoxy curcumin are reported to be

responsible for the yellow colour in some species. The oil contert varies from 1-6.5% and is made of mono and sesquiterpene such as A and B pinene, phellandrene, camphor, camphene, DL-ar-turmerone stain and a, ß curcumenes. Types such as C. angustifolia and C. caulina has high starch and is used instead of the root of the arrow.

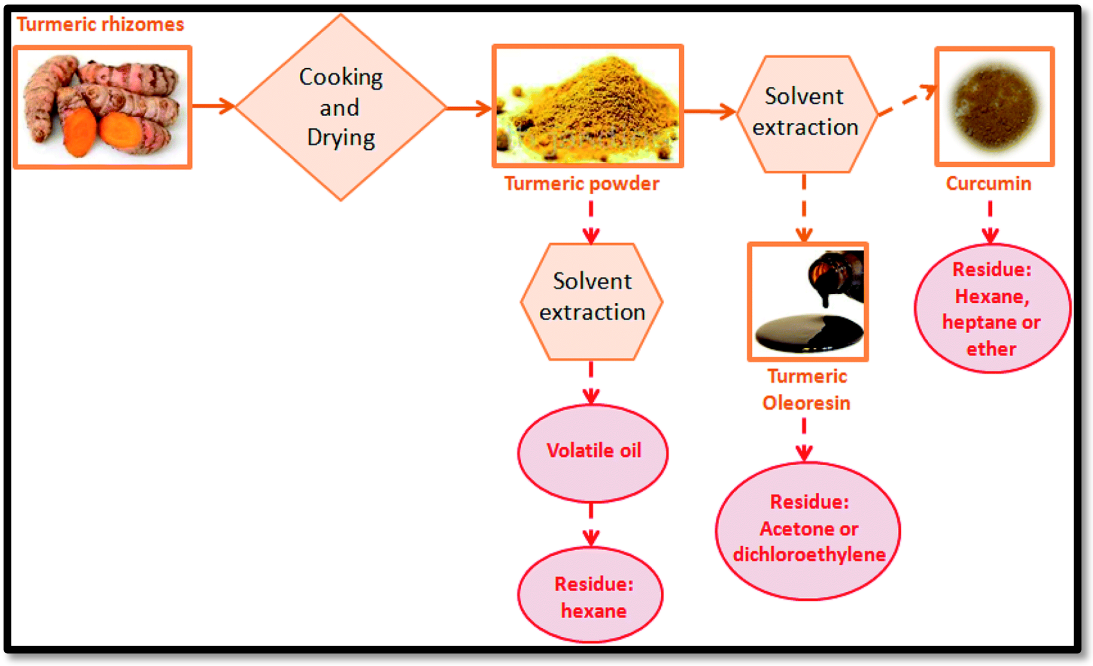
2.1. Consumption and Importance of Curcumin

Turmeric has been put to use as a food-stuff, cosmetic, and medicine. It is widely used as a spice in South Asian and Middle Eastern cooking. It lends curry its distinctive yellow colour and flavour. It is used as a colouring agent in cheese, butter, and other foods (Govindarajan 1980; Ammon and Wahl 1991). As a result of Indian influence, turmeric has made its way into Ethiopian cuisine. In South Africa, turmeric is traditionally used to give boiled white rice a golden color. Turmeric is also used in manufactured food products such as canned beverages, dairy products, baked products, ice cream, yellow cakes, yogurt, orange juice, biscuits, popcorn, sweets, cake icings, cereals, sauces, and gelatines. It is a significant ingredient in most commercial curry powders. Turmeric has numerous uses in Asian cuisine. It is used in savory and sweet dishes, and is widely used in Eastern specialties such as fresh turmeric pickle. The reported consumption of turmeric in Asian countries in humans is in the range of 200–1000 mg/day.

2.2. Extraction of Curcumin from Turmeric

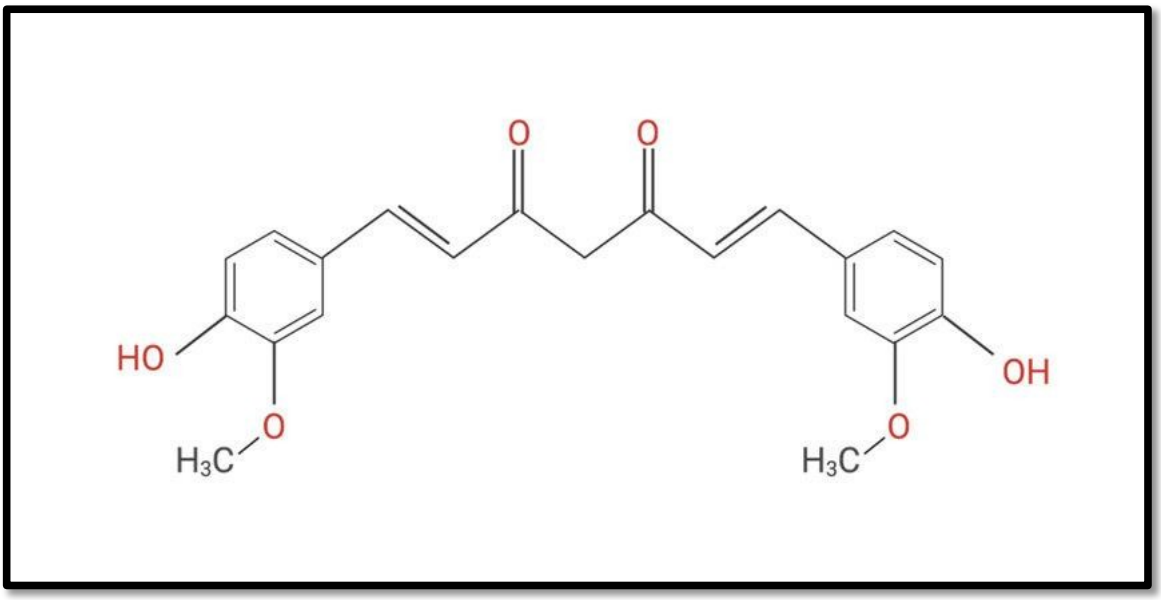
The extract of turmeric has many medicinal properties including antioxidant, anti-inflammatory, antiviral, antibacterial, antifungal, and cancer chemo preventive actions. Curcumin, a yellow compound isolated from its rhizome, may be responsible for the bioactive effects. Recent research shows that curcumin may inhibit carcinogenesis and angiogenesis. They may have a potential to improve chronic inflammatory conditions in obesity. Curcumin is a liposoluble compound and can be easily dissolved into organic solvent such as methanol, ethanol, and acetone. However, poor water solubility often limits its biomedical uses using aqueous systems. This observation prompted us to examine turmeric extracts as a delivery system for curcumin and to examine the possibility of turmeric extract itself as candidate agent for pharmacologic evaluation. In this preliminary study, we used different solvents to extract the crude turmeric material and compared the curcumin concentrations in these extracts. The total of curcuminoids which is about 4-6%, turmeric also contains 2-4% essential oil and 2-3% of fixed oil and various volatile oils, including turmerone, atlantone, and zingiberone. Other constituents include sugars, proteins and resins. The choice of solvents for extraction is restricted to the few solvents of defined purity allowed by national and international food laws in the processing of food materials. Hexane, acetone, alcohol (ethanol, methanol), isopropanol and ethyl acetate are used in the extraction of oleoresins of spices. From consideration of solubility of active constituents, the curcuminoids are poorly soluble in the hydrocarbon solvents. Alcohol and acetone are good extractants and the yields can alsob eexpected to be high because of extraction of non-flavour components. Soxhlet extraction of turmeric powder with acetone gave a yield of about 4.1% containing in 3 hours. Acetone as solvent was slightly superior to alcohol and ethyl acetate, the curcuminoids content also is on the high side, suggesting selective extraction. The results of extraction with acetone have, however been reported to give high yields of curcuminoids than alcoholic and remaining extraction.

Figure 2.2: Bio-refinery of Turmeric

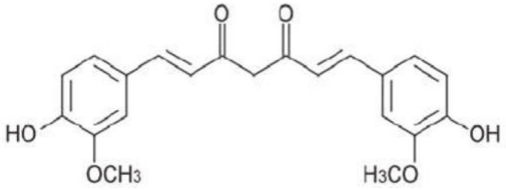


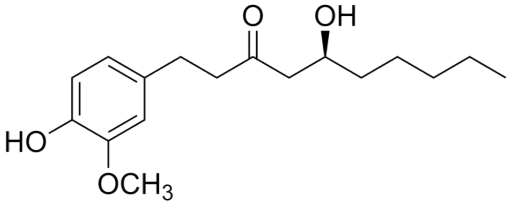
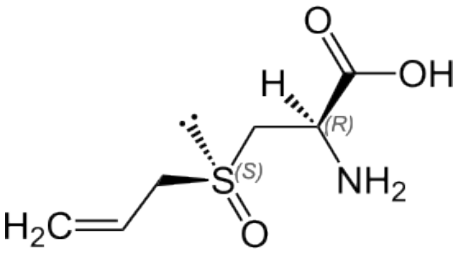
2.3. Structure of Curcumin

Figure 2.3: Structure of Curcumin



Spice Phytoconstituent as an Anti-bacterial Agents

Sr. No.	Spice Chemicals	Source	Structure	Reference
1	Turmeric	Curcum alonga		"Turmeric: The Genus Curcuma". Edited by P.N. Ravindran, K. Nirmal Babu, K. Sivaraman. Boca Raton: CRC Press, 2007.

2	Ginger	Zingiber officinale		"Zingiber officinale". Germplasm Resources Information Network (GRIN). Agricultural Research Service (ARS), United States Department of Agriculture (USDA). Retrieved on 10 December 2017.
3	Garlic	Allium sativum		"Allium sativum L.". Kewscience; Plants of the World Online; Royal Botanic Gardens, Kew, England. Retrieved on 26 May 26 2017.

Positive and Negative Effects of Consumption

The turmeric that we see on shelves and in spice cabinets is made of the ground roots of the plant. The bright yellow color of processed turmeric has inspired many cultures to use it as a dye. Ground turmeric is also a major ingredient in curry powder. Capsules, teas, powders, and extracts are some of the turmeric products available commercially. Curcumin is the active ingredient in turmeric, and it has powerful biological properties. Ayurvedic medicine, a traditional Indian system of treatment, recommends turmeric for a variety of health conditions. These include chronic pain and inflammation. Western medicine has begun to study turmeric as a pain reliever and healing agent.

Positive Effects

- **Its anti-inflammatory:** Several studies in which turmeric has reduced inflammation. This anti-inflammatory ability might reduce the aggravation that people with arthritis feel in their joints. The foundation suggests taking capsules of 400 to 600 milligrams (mg) of turmeric up to three times per day for inflammation relief.
- **It can relieve pain:** Many people, including doctors, cite their own anecdotal experience with turmeric as a pain reliever. The spice is reputed to relieve arthritis pain as well. It seem to support turmeric for pain relief, with one. Source noting that it seemed to work as well as ibuprofen (Advil) in people with arthritis in their knees. Though dosing recommendations seem to vary, those who participated in the study took 800 mg. Trusted Source of turmeric in capsule-form each day.
- **It improves liver function:** Turmeric has been getting attention recently because of its antioxidant abilities. The antioxidant effect of turmeric appears to be so powerful that it may stop. Source your liver from being damaged by toxins. This could be good news for people who take strong drugs for diabetes or other health conditions that might hurt their liver with long-term use.
- **It may help reduce the risk of cancer:** Curcumin shows promise as a cancer treatment. Source suggest it has protective effects against pancreatic cancer, prostate cancer, and multiple myeloma.
- **It can aid your digestion:** Part of the reason that turmeric is in curry powder is because it adds an element of deliciousness to food. But turmeric can also play an important role in digesting that food. Because of its antioxidant and anti-inflammatory properties, turmeric can contribute to healthy digestion. It's used in ayurvedic medicine as a digestive healing agent. Now western medicine has begun to study. Source how turmeric can help with gut inflammation and gut permeability, two measures of your digestive efficiency. Turmeric is even being explored. Source as a treatment for

irritable bowel syndrome.

Negative Effects

- **It can upset your stomach:** The same agents in turmeric that support digestive health can cause irritation when taken in large amounts. Some participants in studies looking at the use of turmeric for cancer treatment had to drop out. Source because their digestion was so negatively affected. Turmeric stimulates the stomach to produce more gastric acid. While this helps some people's digestion, it can really do a number on others.
- **It thins your blood:** Turmeric's purifying properties may also make you bleed more easily. It's not clear why this happens. Other suggested benefits of turmeric, such as lowered cholesterol and lowered blood pressure, probably have something to do with the way turmeric functions in your blood. People who take blood-thinning drugs like warfarin (Coumadin) should avoid. Source consuming large doses of turmeric.
- **It may stimulate contractions:** You may have heard that eating foods seasoned with curry can stimulate labor. Although there's little clinical data to back up this claim. Source suggest turmeric can ease symptoms of PMS. So there may be something to the old wives' tale. Because of its blood-thinning effects alone, pregnant women should avoid taking turmeric supplements. Adding small amounts of turmeric as a spice to food shouldn't be a problem.

Clinical and Pre-clinical Studies

- The clinical pipeline remains insufficient to tackle the challenge of increasing emergence and spread of antimicrobial resistance.
- It is primarily driven by small- or medium-sized enterprises (SMEs), with large pharmaceutical companies continuing to exit the field.
- Eight new antibacterial agents have been approved since 1 July 2017, but overall, they have limited clinical benefits.
- One new anti-bacterial agent, pretomanid, developed by a not-for-profit organization, has been approved for use within a set drug-combination treatment for MDRTB.
- The current clinical pipeline contains 50 antibiotics and combinations (with anew therapeutic entity) and 10 biologicals, of which 32 antibiotics are active against the WHO priority pathogens:
- Six of these agents fulfil at-least one of the innovation criteria; only two of these are active against the critical MDR Gram-negative bacteria.
- More than 40% of the pipeline targeting WHO priority pathogens consists of additional β-lactamand β-lactamase inhibitor (BLI) combinations, with a major gap in activity against metallo-β- lactamase (MBL) producers.
- The antibacterial pipeline is more innovative than the WHO priority. Pathogens pipeline, with more than half of the antibiotics fulfilling all of the innovation criteria.

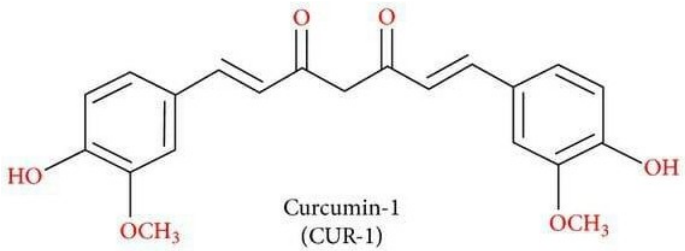
Pharmaco-kinetics and Pharmaco-dynamics

Pharmacokinetic and Pharmacodynamic is the studies of curcumin have been indicated its low intestinal absorption and rapid clearance from the body. Absorption, Metabolism, Biodistribution and excretion of curcumin in rodents have been reported in several studies. The overall findings imply that curcumin has a low absorption and rapid clearance following oral use. In a primary research, a dose of 1g/kg curcumin was administered to rats and resulted in about 75% excretion of curcumin in. It has been reported that, in rats, about 75% of orally administered curcumin is excreted in Faeces. It was

inferred that curcumin was metabolized rapidly in the blood after intravenous Administration. Following ingestion of curcumin in mice, it is Biotransformed first into dihydrocurcumin and Tetrahydrocurcumin. Subsequently, these metabolites are converted to monoglucuronide conjugates. Intraperitoneal (i.p.) injection of curcumin (0.1 g/kg) resulted in a concentration in the plasma of 2.25 µg/mL within the first 15 minutes. One hour after the i.p. injection, the concentrations of Curcumin in the intestines, spleen, liver, and kidneys were 177.0, 26.1, 26.9, and 7.5 µg/g, respectively. Only traces (4.1 µg/g) were found in the brain at 1 Hour. In the plasma, curcumin, tetrahydrocurcumin and two conjugates of curcumin were detected by HPLC. The in vivo bioavailabilty of curcumin following ingestion was considered low by Ammon and Wahl, but others estimated that it was 65%. Interestingly, this bioavailability can be enhanced in humans and rats by concomitant ingestion of piperine (a component of pepper). In patients with Cancer, curcumin and its metabolites were detected in Hepatic tissue and portal blood and in the Colorectum following oral administration of Curcumin at doses of 450–3600 mg daily for 7 days. The authors concluded that a daily dose of 3.6 g Curcumin achieves pharmacologically efficacious levels in the colorectum, with negligible distribution of the compound outside the gut, while the curcumin doses required for the provision of hepatic levels sufficient to exert pharmacological activity are probably not feasible in humans. Curcumin binds with Serumalbumin through hydrophobic interactions, and therefore may be transported to appropriate target cells.

Mechanism of Action of Curcumin as an Anti-bacterial Agents

Curcumin inhibits the growth of both Gram-positive and Gram-negative bacteria. S. aureusisone of the Gram-positive strains that is susceptible to curcumin-mediated inhibition. S. aureusisapathogen that causes various infections including infective endocarditis (IE), bacteremia, skin and soft tissue, osteoarticular, and pleuropulmonary infections. Over the years, S. aureus has evolved and developed multiple strategies to evade human immune system and to resist antibiotics treatment. This has given rise to the evolution of MRSA, and the emergence of healthcare-associated (HA) and community-associated (CA) MRSA has caused a major problem to the human society. In this section, we discuss the past and current works that show the curcumin-mediated killings of MSSA and MRSA. The minimal inhibitory concentrations (MICs) of curcumin against 10 strains of S. aureus (including 2 ATCC MSSA and MRSA standards trains, 4 MRSA clinical isolates, and 4 MRSA from culture collection) ranged from 125 to 250 µg/mL while a study by Wang et al. showed the MIC of 256 µg/mL against MSSA. Using a broth microdilution assay, our group also showed that 250 µg/mL curcumin was required to kill the two ATCC MSSA and MRSA strains. However, another study demonstrated that the MICs against the ATCC standard MSSA and MRSA were 219 and 217 µg/mL, respectively, that are slightly lower than the former study]. Recently, Kali et al. Showed the mean curcumin MICof 126.9 µg/mL against 15 Gram-positive bacterial.



Curcumin-1
(CUR-1)

Conclusion

The previous investigations have shown the extensive antimicrobial activity of curcumin, although in vivo studies in some cases reported the less effective results of curcumin inhibitory effect. Among all former studies on antibacterial activity of curcumin the most promising result is against Helicobacterpylori, at-least for using the curcumin as a complementary compound in combination with other existing medicines to decrease the symptoms of gastritis. Bacterial infections are among the important infectious diseases. Hence, over 50 years of extensive researches have been launched for achieving new antimicrobial medicines isolated from different sources. Despite progress in development of antibacterial agents, there are still special needs to find new antibacterial agents due to development of multidrug resistant bacteria. The antibacterial study on aqueous extract of C. long arhizome demonstrated the MIC (Minimum Inhibitory Concentration) value of 4 to 16 g/L and MBC (Minimum Bactericidal Concentration) value of 16 to 32 g/L against S. epidermiscurcum in showed significant antibacterial activity with MIC values between 5 and 50 µg/mL against 65 clinical isolates of Helicobacterpylori. Curcuminal so has aninhibitory effecton NF-κ Bactivation and as a result on the release of IL-8 and cell scattering which led to a reduction in inflammation of gastric tissue as the main consequence for H. pylori in the stomach. It inhibits the IκBα degradation, the activity of NF-κB DNA-binding and IκB kinase α and β (IKK α and β). Indeed, curcumin inhibited the matrix metalloproteinase-3 and metalloproteinase-9 activity (MMP-3 and MMP-9) as inflammatory molecules involved in H. pylori infection in mice and in cell culture with a dose-dependent manner.

References

1. L.J. Alderwick, J.Harrison, G.S. Lloyd, H.L. Birch. (2015). The Mycobacterial Cell Wall-Peptidoglycan and Arabinogalactan. Cold Spring Harbor Perspectives in Medicine, 5(8), a021113. https://doi.org/10.1101/cshperspect.a021113
2. A. Amalraj, A. Pius, S. Gopi, S. Gopi. (2016). Biological activities of curcuminoids, other biomolecules from turmeric and their derivatives - A review. Journal of Traditional and Complementary Medicine, 7(2), 205-233. https://doi.org/10.1016/j.jtcme.2016.05.005
3. T. Aponte. (2018). Green tea polyphenol EGCG-S as an antimicrobial agent. (Unpublished master's thesis). Montclair State University, Montclair, NJ, 32-36.
4. N.V. Balaji, B.H. Babu, V.U. Rao, G.V. Subbaraju, K.P. Nagasree, M.M.K. Kumar. (2019). Synthesis, Screening and Docking Analysis of Hispolon Pyrazoles and Isoxazoles as Potential Antitubercular Agents. Current Topics in Medicinal Chemistry, 19(1). https://doi.org/10.2174/1568026619666190305124954
5. B.B. Aggarwal, Y. Takada, O.V. Oommen. From Chemoprevention to Chemotherapy: Common Targets and Common Goals. Expert Opin. Investig. Drugs, 2004, 3, 1327–1338.
6. Alam M.A, Ali N.A, Sultana N. et al. Newborn umbilical cord and skin care in Sylhet District, Bangladesh: Implications for the promotion of umbilical cord cleansing with topical chlorhexidine. J. Perinatol, 2008, 28, S61–S68.
7. Amara A.A, El-Masry M.H, Bogdady H.H. Plant crude extracts could be the solution: Extracts showing invivo antitumorigenic activity. Pak. J. Pharm. Sci, 2008, 21, 159–171.
8. Ammon H.P, Wahl M.A. Pharmacology of Curcuma longa. Planta Med., 1991, 57, 1–7.
9. V. Lampe, J. Milobedeska. Studien über curcumin. Ber Dtsch Chem Ges, 1913, 46, 2235-2240.
10. A.M. Anderson, M.S. Mitchell, R.S. Mohan. Isolation of curcumin from turmeric. J. Chem. Educ., 2000, 77, 359-360.
11. Ah. L. Haque, K.A. Saleem. Separation and identification of curcuminoids in turmeric powder

by HPIC using phenyl column. Anal. Methods, 2014, 6, 2526-2536.
12. X. Sun, C. Gao, W. Cao, X. Yang, E. Wang. Capillary elelctrophoresis with amperometric detection of curcumin in Chinese herbal medicine pretreated by solid-phase extraction. J. Chromatogr. A., 2002, 962, 117-125.
13. International standards for clinical trial registries – Version 3.0. Geneva: World Health Organization, 2018.
14. Antibacterial agents in clinical development. Geneva: World Health Organization, 2018.
15. C. Pulcini, K. Bush, W.A. Craig, N. Frimodt-Møller, M.L. Grayson, J.W. Mouton et al. Forgotten antibiotics: An inventory in Europe, the United States, Canada and Australia. Clin. Infect. Dis., 2012, 54, 268–274.
16. H.H. Tonnesen, J. Karlsen, G.B. van Henegouwen. Studies on Curcumin and Curcuminoids VIII. Photochemical Stability of Curcumin. Z. Lebensm. Unters. Forsch., 1986, 183, 116-122.
17. https://www.researchgate.net/figure/Molecular-structure-of-curcumin-Curcumin-is-a-symmetric-molecule-with-chemical-formula_fig1_339667053
18. https://www.medicalnewstoday.com/articles/318405
19. T. Esatbeyoglu, P. Huebbe, M.A. Insa, E. Dawn Chin, A.E. Wagner, G. Rimbach. Curcumin From Molecule to Biological Function. Angew. Chem. Int. Ed., 2012, 51, 5308-5332.
20. Y.J. Kim, H.J. Lee, Y. Shin. Optimization and validation of high-performance liquid chromatography method for individual curcuminoids in turmeric by heat-refluxed extraction. J. Agric. Food Chem., 2013, 61, 10911-10918.
21. N. Kurmudle, L.D. Kagliwal, S.B. Bankar, R.S. Singhal. Enzyme-assisted extraction for enhanced yields of turmeric oleoresin and its constituents. Food Biosci., 2013, 3, 36-51.
22. Medically reviewed by Debra Rose Wilson, Ph.D., MSN, R.N., IBCLC, AHN-BC, CHT-By Kathryn Watsonon 12 July 2017
23. https://www.medicalnewstoday.com/articles/318405
24. Pan M.H., Huang T.M., Lin J.K. Biotransformation of curcumin through reduction and glucuronidation in mice. Drug Metab. Dispos.,1999, 27, 486–494.
25. Ireson C.,Orr S., Jones D.J. Characterization of metabolites of the chemopreventive agent curcumin in human and rat hepatocytes and in the rat in vivo, and evaluation of their ability to inhibit phorbolester-induced prostaglandin E2 production. Cancer Res., 2001, 61, 1058–1064.
26. B. Chandran, A. Goel. A randomized, pilot study to assess the efficacy and safety of curcumin in patients with active rheumatoid arthritis. Phytother Res Phytother Res., 2012, 26(11), 1719–1725.
27. Phytosomal curcumin: A review of pharmacokinetic, experimental and clinical studies. https://doi.org/10.1016/j.biopha.2016.11.098
28. By Atli Arnarson, B.Sc., Ph.D. — Medically reviewed by Amy Richter, RD, Nutrition. https://www.healthline.com/nutrition/turmeric-side-effects
29. M. Collin, N.S. Patel, L. Dugo, C. Thiemermann. Role of peroxisome proliferator-activated receptor-γ in the protection afforded by 15-deoxyΔ12,14 prostaglandin J2 against the multiple organ failure caused by endotoxin. Critical Care Medicine, 2004, 32(3), 826–831.
30. M. Abdelrahman, M. Collin, C. Thiemermann. The peroxisome proliferator-activated receptor-γ ligand 15-deoxy Δ12,14 prostag landin J2 reduces the organ injury in hemorrhagic shock. Shock, 2004, 22(6), 555–561.