

Bioactive compounds of turmeric and their pharmacological effects

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Abstract. Turmeric has various biological compounds. It has been used as a spice in most Asian countries. Both solid and powder extracts, as well as extracts in oil form, are beneficial. Moreover, having an abundant number of biological compounds made it popular in ancient times. For centuries, it has been used to treat wounds and snake bites. The main component of turmeric is curcuminoids, which are reported to have anti-cancer, anti-diabetic, and anti-tumor activities. In recent decades, many studies have taken place for clinical trials to confirm curcumin's pharmacological activity. In this review, turmeric constituents and the therapeutic activity of curcumin analogs will be discussed.

Keywords: Biological activity, biological compounds, curcumin derivatives, pharmacological properties

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1. Introduction

Curcuma longa (Linn.) is a long-lasting rhizomatous plant in the Zingiberaceae family, generally called turmeric. It can grow up to 5 feet in height and has lanceolate-shaped leaves and yellowish funnel-shaped blooms. Turmeric can be grown in a variety of environments with temperatures ranging from 20 to 35 °C and about 1.5 cm of yearly rainfall. It has been observed in the development of rich, sandy, or clay-enriched soils where there is no water pooling or puddling. Ahmad et al. (2020) said that for good organic products, the pH range of the soil should be between 4.75 and 7.5.

Turmeric is famous as a spice in Southeast Asia and is frequently used in local cuisines. Globally, it is also used as an edible color and to conserve food products (Paramasivam et al., 2009). In curries and mustards, the powder is widely used to impart color and flavor. It helps to maintain freshness and nutritional values and improve the deliciousness of the food. Furthermore, it has been utilized in South Asian countries for dental hygiene (Chaturvedi, 2009). Turmeric is available as powders, pastes, capsules, and tablets to be used as food supplements. Moreover, it is widely used in energy drinks, soaps, and cosmetics.

Turmeric is one of the most widely used traditional plants and has been used for hundreds of years in Indo-Chinese herbal medicine for its variety of properties, e.g., anti-inflammatory, wound healing, liver tonic, and anti-tumor activity (Huang et al., 2018). The importance of this root has expanded due to the presence of bioactive chemicals known as curcuminoids (the main family of phenolic compounds present in turmeric) (Munekata et al., 2021). Curcuminoids have been found in more than 100 different curcuma species, such as *C. phaeocaulis*, *C. aromatica*, *C. xanthorrhiza*, *C. zedoaria*, and *C. mangga* (Aggarwal et al., 2007).

Curcumin supplementation appears to have a plethora of therapeutic benefits; most of them are attributable to its anti-oxidant properties and the capacity to reduce inflammation (Hewlings & Kalman, 2017). It has long been used in Ayurvedic medicine for a wide range of biological properties, e.g., including anti-oxidant, anti-inflammatory, anti-carcinogenic, analgesic, chemopreventive, anti-septic, chemotherapeutic, anti-platelet, anti-viral, anti-bacterial, anti-fungal, and anti-tumor activity (Sandur

et al., 2007; Prakash et al., 2011). Singh et al. (2010) also found that the essential oil made from turmeric has anti-fungal, anti-hepatotoxic, and anti-arthritic properties. So, this review talked about the bioactive compounds in turmeric and how they work in the body.

2. Bioactive compounds of turmeric

The main phytoconstituents in turmeric are dihydroheptanoids, also known as curcuminoids, which comprise around 16% of the dry weight of turmeric (Niranjan et al., 2018). Curcumin, also called diferuloylmethane, is a key component in turmeric that can be obtained after solvent extraction and crystallization (Amalraj et al., 2017). Furthermore, it accounts for 2–8% of all turmeric components, is thought to be the primary origin of turmeric's yellow or golden color, and has also been linked to many of the spice's qualities (Ruby et al., 1995; Mansouri et al., 2020). It does not dissolve in water or ether, but ethanol and other organic solvents can break it up (Aggarwal et al., 2003).

The most important curcuminoid complexes are curcumin I, curcumin II, and curcumin III (Ahmad et al., 2020). Curcumin's naturally occurring curcuminoids ratios are about 5% bisdemethoxycurcumin (Cur-III) and 15% demethoxycurcumin (Cur-II) (Ireson et al., 2001) (Figure 1). Curcumin is the most abundant biologically active molecule in turmeric and a well-studied physiologically active molecule with anti-oxidant and anti-inflammatory properties (Ahmed & Gilani, 2009). Additionally, the demethoxy derivatives of curcumin and several polypeptides having anti-oxidant effects, such as turmerin, are other major bioactive ingredients in turmeric (Ramírez-Tortosa et al., 1999).

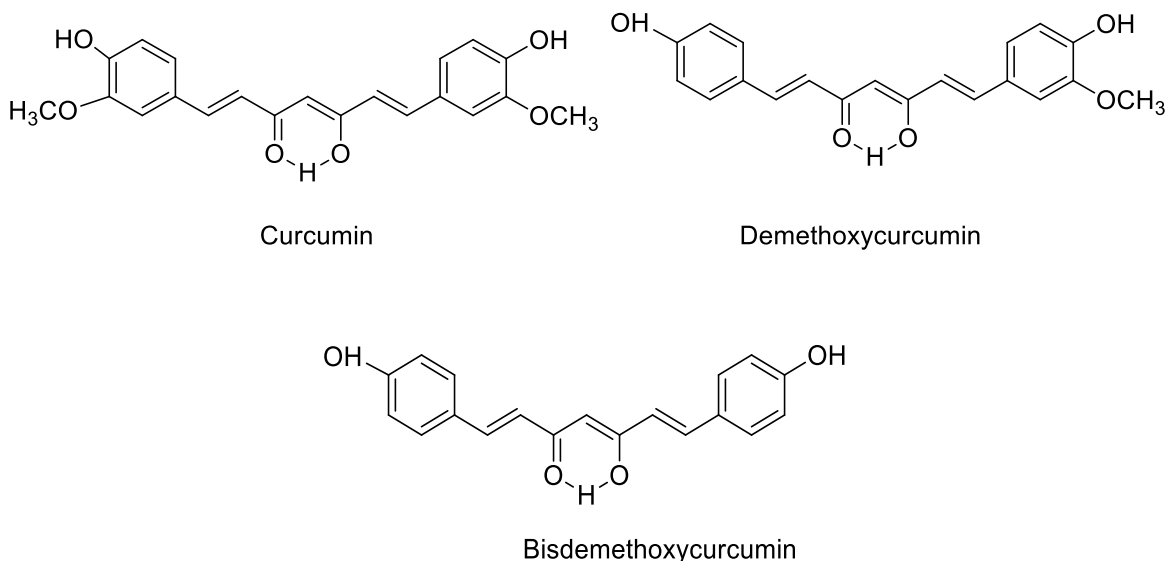


Figure 1. Chemical structures of curcumin, demethoxycurcumin, and bisdemethoxycurcumin (ChemDraw)

3. Pharmacological properties of turmeric

As described earlier, turmeric has been utilized for treatments in traditional medicine systems for hundreds of years due to its wide range of biological properties and non-toxic nature. The essential oil in turmeric has also been shown to help with arthritis, inflammation, and fungal infections (Table 1).

3.1. Anti-arthritis effects

Curcumin has been demonstrated to have anti-arthritic properties in patients with osteoarthritis and rheumatoid arthritis in several investigations (Henrotin et al., 2013). Moreover, a combination of curcumin, vitamin D3, and omega-3 fatty acids significantly delayed the onset and severity of collagen-induced arthritis (Hemshekhhar et al., 2021). Notably, analgesics, steroids, and non-steroidal anti-inflammatory medications (NSAIDs) are currently used to treat arthritis, and they alleviate symptoms such

as extreme pain and inflammation (Daily et al., 2016). Paultre et al. (2021) said that turmeric therapy for pain and function might work as well as NSAID therapy.

3.2. Anti-cancer activity

Turmeric and its constituents are multi-targeted phytochemicals that can be used to fight cancer. Their use can reduce uncontrolled cell proliferation, inflammation, angiogenesis, and metastasis while improving apoptosis, autophagy, and cell cycle arrest by modulating various cell signaling pathways (Aggarwal et al., 2003; Kasi et al., 2016; Zhu & Bu, 2017; Song et al., 2019; Hassanzadeh et al., 2020). The influence of curcumin on Wilm's tumor 1 (WT1) gene expression in leukemic K562 cells was studied and found to be mediated via PKCa signaling upstream of WT1 transcription factor auto-regular function (Semsri et al., 2011).

3.3. Anti-diabetic effects

Curcumin has been proven to have promising anti-diabetic effects. It also lowers fasting blood glucose, glycated hemoglobin, and body mass index considerably (Marton et al., 2021). Curcumin treatment for pre-diabetic people can reduce their chance of developing type 2 diabetes by up to 50% (Chuengsamarn et al., 2012). Curcumin may also be a viable option for preventing and treating diabetes and its consequences, such as diabetic retinopathy (Li et al., 2015). Moreover, significant plasma lipid and cholesterol-lowering activity by nanocurcumin was previously reported (Marton et al., 2021).

3.4. Anti-fungal activity

Due to turmeric's traditional worldwide use in food products, many studies have been conducted to investigate the fungus's static and anti-infective activity. Turmeric oil derived from *Curcuma longa* is reported to possess anti-fungal properties (Aggarwal et al., 2007). Curcumin has also been shown to have anti-influenza activity (Chen et al., 2010). For example, treatment with 30 M curcumin reduced viral production in cell culture by more than 90%, according to their findings. Moreover, *C. longa* hexane extract at 1000 µg/mL showed antifungal activity against several fungus varieties (Moghadamtousi et al., 2014).

3.5. Anti-inflammatory activity

Curcuminoids and turmeric oils have anti-inflammatory properties. Chemicals extracted from turmeric rhizomes are reported to be potent inhibitors of inflammatory mediator synthesis (Lantz et al., 2005). It suppressed inflammation primarily through the Wnt/beta-catenin and nuclear factor kappa B (NF-B) pathways (Suresh et al., 2019).

3.6. Anti-microbial activity

Turmeric has been found to have bacteriostatic properties. Curcumin has anti-bacterial properties against *S. aureus*, irrespective of its methicillin resistance capacity (Teow et al., 2016). In another study (Parvathy et al., 2009), it was also found that curcumin-diglucoside could kill germs. In a trial of *Eimeria maxima* infected chicks, meals supplemented with 1% turmeric reduced intestinal lesions and enhanced weight gain (Kwon & Magnuson, 2009). Another animal study found that applying turmeric oil topically to guinea pigs for 7 days prevented the growth of dermatophytes and dangerous fungi (Dujic et al., 2009). Curcumin also has some action against *Plasmodium falciparum* and *Leishmania* major organisms (Huang et al., 1998).

3.7. Antioxidant activity

Curcuminoids have been shown to have potent anti-oxidant action in a variety of chemical *in vitro* assays as well as in several *in vivo* studies. Turmeric extract has been demonstrated to have significant anti-oxidant activity in 2,2'-azinobis-(3-ethylbenzothiazoline-6-sulfonic acid) (ABTS) and 2,2-diphenyl-1-picrylhydrazyl (DPPH) radical-scavenging activity tests (Lee et al., 2015). Anti-oxidant properties are also seen in curcumin derivatives such as bisdemethoxycurcumin and demethoxycurcumin (Ammon et al., 1992). For example, in HepG2 cells, the anti-oxidant properties of turmeric led to lower levels of prostaglandin E2, which is a sign of oxidative stress (Menghini et al., 2010).

3.8. Anti-platelet properties

Curcuma oil has anti-platelet properties in experimental models of cardiac ischemia-reperfusion and thrombosis (Prakash et al., 2011). The effect of water-dispersible curcuminoids on rat platelet aggregation was evaluated and found to be two times

more effective at inhibiting platelet aggregation than curcumin in their studies ([Maheswaraiah et al., 2015](#)). In addition, turmeric oil is reported to show anti-platelet activity ([Daveluy et al., 2014](#)).

3.9. Cardio-protective effect

Curcumin is a cardioprotectant that can protect cardiomyocytes. It protected H9c2 cells from hypertrophic stress and helped to maintain the extracellular matrix. It increased the amount of collagen by reducing the production of an enzyme responsible for the breakdown of collagen ([Kohli et al., 2013](#)). In addition, curcumin inhibited histone acetyltransferases to prevent atypical enlargement of the heart muscle, which aided in reducing the possibility of cardiac failure ([Morimoto et al., 2008](#)).

3.10. Gastrointestinal and hepatic effects

Curcumin may be particularly well adapted to being developed to treat gastrointestinal illnesses due to its enhanced bioavailability in the gastrointestinal tract. Curcumin has been recommended as a treatment for liver and digestive illnesses such as IBS, colitis, and bacterial and parasitic infections ([Hassanzadeh et al., 2020](#)). The primary fibrogenic cell in the liver, the hepatic stellate cell (HSC), is implicated in fibrosis, creating scar tissue in response to liver injury ([Xu et al., 2018](#)). For example, curcumin administration has been shown to impair HSC viability by suppressing proliferation and increasing endoplasmic reticulum stress ([Chen et al., 2014](#)). Turmeric compounds, mainly curcumin, have significant effects in treating fatty liver disease. Curcumin is reported to be effective against nonalcoholic fatty liver disease models, such as nonalcoholic steatohepatitis (NASH) ([Zabihi et al., 2017](#)). For instance, when taken orally, curcumin efficiently protected against the progression of non-alcoholic fatty liver disease caused by a high-fat diet by altering metabolism and increasing intrahepatic CD4+ cell accumulation ([Inzaugarat et al., 2017](#)). In addition, the effect of curcumin extract is reported to decrease the severity of alanine transaminase, aspartate transaminase, and non-alcoholic fatty liver disease ([Rolfe et al., 2020](#)).

3.11. Neuroprotective effect

Curcumin has been shown to have neuroprotective activity, possibly due to its anti-oxidant and anti-inflammatory properties, which aid in maintaining biochemical balance in the brain ([Dikmen et al., 2017](#)). It has a lot of qualities that make it an excellent neuroprotective medication ([Cole et al., 2007](#)). It has been studied as a possible treatment for a variety of neurological illnesses, including Parkinson's disease and Alzheimer's disease (AD) ([Teter et al., 2019](#)). According to research from Grundman et al. (2002), curcumin also reduces inflammation and oxidative damage in mouse models of Alzheimer's disease.

3.12. Radioprotective or radiosensitizing effect

Curcumin has radioprotective and radiosensitizing properties. Curcuminoids are polyphenols that impart radioprotective effects on healthy cells and radiosensitizing effects on cancer cells due to their anti-oxidant activity. For example, curcumin showed protective effects on parotid glands during a radiotherapy study in a rat model ([Lopez-Jornet et al., 2016](#)). Moreover, curcumin's radiosensitizing effect on breast cancer cells has been reported ([Minafra et al., 2019](#)).

3.13. Wound-healing properties

Curcumin has been used traditionally for wound healing. Curcumin's capacity to stimulate granulation tissue formation, tissue remodeling, collagen deposition, and wound contraction has proven that it has significant wound healing properties ([Akbik, 2014](#)). For example, in a clinical trial, curcumin improved topical wounds in rats and guinea pigs by boosting granulation tissue formation, extracellular matrix protein production, and TGF-1 levels in wounds ([Sidhu et al., 1998](#)). In addition, systemic administration of curcumin after muscle injury resulted in quick recovery by tissue regeneration ([Thaloor et al., 1999](#)).

Table 1. List of curcumin derivatives and their biological activities

Sl	Compound Name	Biological activity	Reference
1	Ar-turmerone	Snakebite	(Ferreira et al., 1992)
2	bisdemethoxycurcumi	Anti-oxidant	(Jayaprakasha et al., 2006)
3	Curcuminoids	Anti-acidogenic activity	(Pandit et al., 2011)
4	Curcuminoids	Anti-cancer activity	(Wei et al., 2021)

Sl	Compound Name	Biological activity	Reference
		(Prostate cancer)	
5	Curcuminoids	Anti-bacterial activity	(Teow et al., 2016)
6	Curcuminoids	Anti-fungal activity	(Aggarwal et al., 2007)
7	Curcuminoids	Anti-viral activity	(Hergenhahn et al., 2002)
8	Curcuminoids	Dentistry	(Chaturvedi, 2009)
9	Curcuminoids	Anti-Alzheimer's	(Grundman et al., 2002)
10	Curcuminoids	Anti-Parkinson's	(Teter et al., 2019)
11	Curcuminoids	Anti-arthritis	(Funk et al., 2010)
12	Curcuminoids	Anti-oxidant activity	(Ammon et al., 1992)
13	Curcuminoids	Anti-angiogenic	(Lal et al., 2016)
14	Curcuminoids	Hypoglycemic	(Kuroda et al., 2005)
15	Curcuminoids	Anti-inflammatory	(Saw et al., 2010)
16	Curcuminoids	Anti-malarial	(Mishra et al., 2008)
17	Curcuminoids	Anti-diabetic	(Chuengsamarn et al., 2012)
18	Curcuminoids	Anti-protozoan	(Changtam et al., 2010)
19	Curcuminoids	Wound healing	(Hegge et al., 2011)
20	Curcuminoids	Anti-depressant	(Kulkarni et al., 2008)
21	Curcuminoids	Anti-venom	(Gomes et al., 2010)
22	Curcuminoids	Anti-tumor activity	(Simoni et al., 2008)
23	Curcumin- β -D-glucoside	Anti-mutagenic	(Parvathy et al., 2009)
24	Curcumin- β -D-glucoside	Anti-oxidant	(Parvathy et al., 2009)
25	Curcumin- β -D-glucoside	Anti-bacterial	(Parvathy et al., 2009)
26	4-hydroxy-3-methoxy-benzylidene derivative	Anti-malarial activity	(Mishra et al., 2008)
27	Methylcurcumin	Leishmaniasis	(Araujo et al., 1999)
28	3-nitrophenylpyrazole curcumin	Anti-malarial activity	(Mishra et al., 2008)
29	Pyrazole curcumin	Anti-malarial activity	(Mishra et al., 2008)
30	Sodium curcumin	Anti-inflammatory	(Mukhopadhyay et al., 1982)
31	Turmerin	Anti-oxidant activity	(Ramírez-Tortosa et al., 1999)

4. Conclusion and future perspectives

Turmeric has been popular all over the world as a spice. It has been used in traditional medicine, especially in Asian countries. It has anti-cancer, anti-bacterial, anti-inflammatory, anti-diabetic, and anti-arthritis properties, as well as wound healing activity. However, scientific evidence on the *in vivo* toxicity, clinical studies, and nutritional value of this plant is still insufficient, especially for high mortality diseases such as cancer. Further research is required to fully understand the cell signaling pathways and genes involved in the anti-cancer activity of curcumin. Moreover, new curcumin analogs can be developed to improve their bioavailability, aqueous solubility, absorption, and bioactivities. So, future studies may focus on finding new and different ways that turmeric can be used as a medicine.

Conflicts of interest. There are no conflicts of interest.

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