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Bioactive compounds of turmeric and their pharmacological effect

Alfi Shahrin[1,2*], Chadni Akter[3], Sabrin Islam Khan[4], and Reatul Karim[1*]
[1]Department of Pharmacy, East West University, Dhaka, Bangladesh.
[2]Incepta Pharmaceuticals, Dhaka, Bangladesh.
[3]Department of Botany, Titumir College, Dhaka, Bangladesh.
[4]Department of Pharmaceutical Sciences, North South University, Dhaka, Bangladesh.
**Corresponding authors' email addresses: 2018-1-70-021@std.ewubd.edu (A.S.), drtk@ewubd.edu (R.K.)*

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Abstract. Turmeric has various biological compounds. It has been used as spices in most Asian countries. Both solid and powder extracts as well as oil form has an advantageous effect. 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; have lanceolate-shaped leaves and yellowish funnel-shaped blooms. Turmeric can be grown in a variety of environments with temperatures ranging from 20-35 °C and about 1.5 cm yearly rainfall. It has been seen in the development of rich in sandy or clay-enriched soils where water pooling or puddling has not occurred. Additionally, the pH range of the soil should be 4.75-7.5 to produce quality organic products (Ahmad et al., 2020).

Turmeric is famous as a spice in South-East 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 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). More than a hundred curcuma species, including C. *phaeocaulis*, C. *aromatica*, C. *xanthorrhiza*, C. *zedoaria*, and C. *mangga*, have been shown to contain curcuminoids (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). In addition, anti-fungal, anti-hepatotoxic, and anti-arthritic properties are all present in the essential oil derived from turmeric (Singh et al., 2010).

2. Bioactive compounds of turmeric

The main phytoconstituents in turmeric are diarylheptanoids, 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 to 8% of all turmeric components, is thought to be the primary origin of turmeric's yellow/golden color, and has also been linked to many of the spice's qualities (Ruby et al., 1995; Mansouri et al., 2020). It has been found as water and ether insoluble but can be dispersed in ethanol and other organic solvents (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% demethoxy curcumin (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).

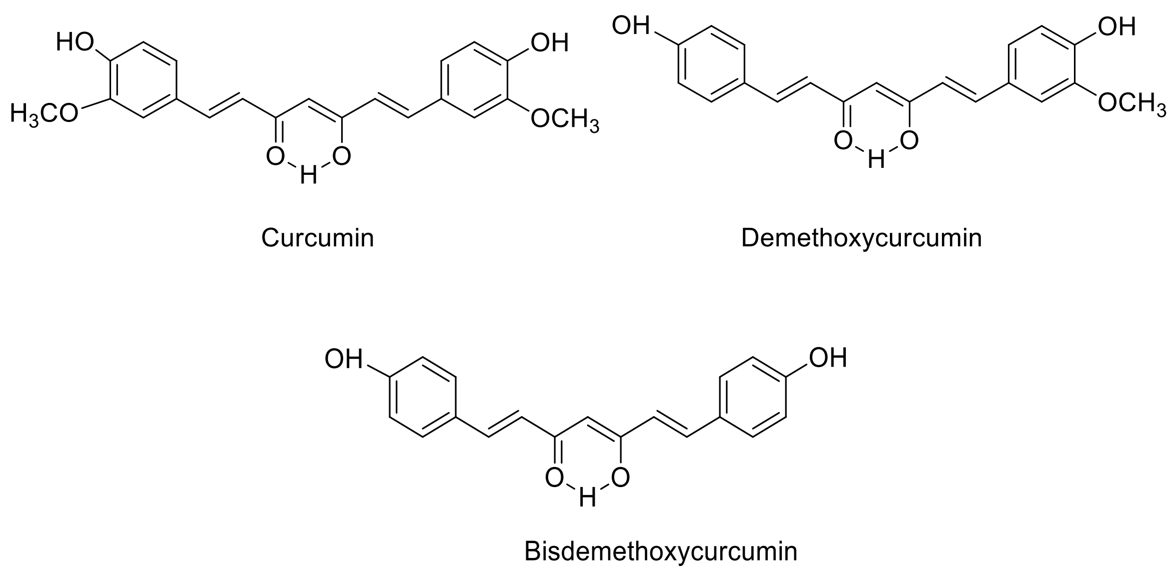

Figure 1. Chemical structures of Curcumin, Demethoxycurcumin, and Bisdemethoxycurcumin (ChemDraw)

3. Pharmacological properties of turmeric

As described earlier, turmeric is being utilized for treatments in traditional medicine systems for hundreds of years due to its wide range of biological properties and non-toxic nature. In addition, the essential oil contained in turmeric showed anti-inflammatory, anti-fungal, anti-arthritic, and other biological activities (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 (Hemshekhar 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). Turmeric therapy for pain and function has been suggested to have similar efficacy to NSAID therapy (Paultre et al., 2021).

3.2. Anti-cancer activity

Turmeric and its constituents are multi-targeted phytochemicals that can be used to fight against 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-regularly 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 nano curcumin were reported previously (Marton et al., 2021).

3.4. Anti-fungal activity

Due to the traditional worldwide usage of turmeric in food products, many studies have been conducted to investigate fungi's static and anti-infective activity of turmeric or curcumin. Turmeric oil derived from *Curcuma longa* is reported to possess anti-fungal properties (Aggarwal et al., 2007). Moreover, it has been investigated that curcumin showed 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 showed anti-inflammatory properties primarily through modulation of the Wnt/-catenin and nuclear factor-kappa B (NF-κB) 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). Moreover, curcumin-β-diglucoside showed anti-microbial properties in another study (Parvathy et al., 2009). In a trial of *Eimera 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. Anti-oxidant 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 instance, in HepG2 cells, turmeric's anti-oxidant activity resulted in lower levels of prostaglandin E2 (an oxidative stress marker) (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 cardio protectant that can protect cardiomyocytes. It protected H9c2 cells from hypertrophic stress and helped to maintain the extracellular matrix. It increased collagen amount 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 to reduce 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 parasite 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 non-alcoholic 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 is reported to show neuroprotective activity possibly by its anti-oxidant and anti-inflammatory properties which helped to maintain biochemical equilibrium 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). In addition, curcumin has been found to lower inflammation and oxidative damage in mice models of Alzheimer's disease (Grundman et al., 2002).

3.12. Radioprotective or radiosensitizing effect

Curcumin has radioprotective and radiosensitizing properties. Curcuminoids are polyphenols imparting 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 in 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 proved 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 in muscle injury resulted in a quick recovery by tissue regeneration (Thaloor et al., 1999).

Table 1. List of curcumin derivatives and their biological activity

SI	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-arthritic	(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 curcuminate	Anti-inflammatory	(Mukhopadhyay et al., 1982)
31	Turmerin	Anti-oxidant activity	(Ramírez-Tortosa et al., 1999)

6. 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 a wound healing activity. However, scientific evidence on *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. Therefore, future research might be based on new and various types of therapeutic activity of turmeric.

Conflicts of interest. There are no conflicts of interest.

ORCID

Alfi Shahrin: https://orchid.org/0000-0003-2116-8171
Chadni Akter: https://orchid.org/0000-0001-8971-8905
Reatul Karim: https://orchid.org/0000-0002-2511-2346

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