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Review article

Major phytoconstituents of *temulawak* (*Curcuma xanthorrhiza*) in hepatoprotective activity

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Abstract. *C. xanthorrhiza*, commonly known as Javanese turmeric or *temulawak* in Indonesia, belongs to the Zingiberaceae family. *C. xanthorrhiza* is widely used to treat various health problems, including loss of appetite, gastrointestinal disorders, constipation, diarrhea, fever, arthritis, and liver dysfunction. In Indonesia, *C. xanthorrhiza* is widely recognized and traditionally used for liver disease treatment, although its hepatoprotective mechanisms were not scientifically validated in traditional practice. Current research has identified xanthorrhizol and curcuminoids (including curcumin and bisdemethoxycurcumin) as the primary active compounds in *C. xanthorrhiza*, which exert hepatoprotective effects through various studied mechanisms.

Keywords. *C. xanthorrhiza*, Curcuminoid, Liver disease, *Temulawak*, Xanthorrhizol.

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1. Introduction

Chronic liver disease has emerged as a leading cause of mortality, particularly in developing countries. Recent years have witnessed a significant increase in its prevalence. In developed nations, the majority of chronic liver diseases comprise alcoholic liver disease, chronic viral hepatitis (including hepatitis B and C), non-alcoholic fatty liver disease (NAFLD), and hemochromatosis [1,2].

Multiple signaling pathways that contribute to tumor development have been identified, presenting opportunities for targeted therapies that can specifically target the components involved in carcinogenesis [3,4]. In conventional medicine, surgical resection, liver transplantation, radiofrequency, chemotherapy, and targeted molecular therapy are the primary approaches used to treat liver cancer [5]. However, recurrence of the disease and drug toxicity or ineffectiveness, which can adversely affect the patient's quality of life after therapy, remain major challenges. Chemotherapy, for example, is often associated with severe side effects that can interfere with treatment. Although sorafenib was generally well-tolerated, toxicities were mild to moderate in severity and included hypertension, hemorrhage, neuropathy, leukopenia, lymphopenia, diarrhea, nausea, vomiting, and dyspnea [6,7]. Furthermore, repeated use of transarterial chemoembolization (TACE) has been linked to fibrosis, toxicity, and hypofunction of the liver [8].

In Indonesia, *Curcuma xanthorrhiza* is commonly used in traditional medicine for liver disease treatment. This herbal practice has been passed down through generations, with its application based primarily on empirical evidence of therapeutic effects rather than specific knowledge of its pharmacological mechanisms. *C. xanthorrhiza*, commonly known as Javanese turmeric or *temulawak* in Indonesia, belongs to the Zingiberaceae family [9]. It is found both in the wild and under cultivation throughout Indonesia and has long been used in traditional medicine. In addition to its medicinal applications,

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C. xanthorrhiza is also commonly consumed as a health tonic [10].

Although *C. xanthorrhiza* belongs to the same family as turmeric (*C. longa*), it is not as widely known or used outside of Indonesia. The two species exhibit notable differences in rhizome characteristics, including size, color, and odor. The rhizomes of *C. xanthorrhiza* are typically larger than those of *C. longa*. In terms of coloration, *C. longa* exhibits a brighter and more intense yellow–orange hue, while *C. xanthorrhiza* tends to have a duller color. Regarding aroma, *C. xanthorrhiza* possesses a more pungent and distinctive odor compared to *C. longa*.

Due to these differences, particularly in odor and color, *C. xanthorrhiza* is predominantly used for medicinal purposes, such as in traditional herbal formulations (*jamu*), rather than in culinary applications. In contrast, *C. longa* is widely used both as a medicinal ingredient and a culinary spice. The strong and distinctive smell of *C. xanthorrhiza* is considered to reduce the sensory appeal of food, limiting its use in cooking.

C. xanthorrhiza is widely used to treat various health conditions, including loss of appetite, gastrointestinal disorders, constipation, diarrhea, fever, arthritis, and liver dysfunction. Compared to *C. longa*, *C. xanthorrhiza* is more frequently utilized in herbal products and traditional medicines as a source of curcumin. Several studies have reported a range of biological activities associated with *C. xanthorrhiza*, including antimicrobial, antibacterial, antinociceptive, antioxidant, anticancer, and anti-inflammatory effects [11,12]. These pharmacological properties are largely attributed to its major bioactive constituents, particularly curcuminoids and xanthorrhizol. Curcuminoids, which belong to the diarylheptanoid class of compounds, include curcumin, demethoxycurcumin, and bisdemethoxycurcumin, each of which is present in *C. xanthorrhiza* [13].

C. xanthorrhiza is a medicinal plant that plays a significant role in promoting health. However, despite belonging to the same family as *C. longa*, the two species are not closely related in terms of phytochemical composition and usage. Scientific publications specifically focused on *C. xanthorrhiza* remain limited across major academic databases. Given the scarcity of existing literature, this review aims to provide a comprehensive overview of *C. xanthorrhiza*, with an emphasis on its distribution, cultivation practices, botanical characteristics, nutritional composition, phytochemistry, traditional and medicinal uses, as well as its pharmacological activities and safety profile.

2. Botanical description, geographical distribution, and cultivation of *C. xanthorrhiza* Roxb.

C. xanthorrhiza is a plant native of Indonesia and is commonly found growing wild in forested areas, particularly under the shade of teak trees. It is widely distributed across several Indonesian islands, including Java, Maluku, and Kalimantan, and is also found in other Southeast Asian countries, as well as in India and China [14]. Taxonomically, *C. xanthorrhiza* belongs to the kingdom Plantae, division Magnoliophyta, class Liliopsida, order Zingiberales, family Zingiberaceae, and genus *Curcuma*, with the species designation *Curcuma xanthorrhiza* Roxb [15,16]. The taxonomic classification of *C. xanthorrhiza* is shown in Figure 1.

C. xanthorrhiza is a perennial herbaceous plant that grows in clumps, with each clump consisting of several shoots. Each shoot typically bears two to nine leaves. The leaves are oval, elongated, or lanceolate in shape, and range in color from green to light or dark purplish brown, often marked with brown stripes. They measure approximately 31–84 cm in length and 10–18 cm in width. The leaves are complete, consisting of a leaf sheath, petiole, and leaf blade. The plant features a pseudostem, from which flowers emerge once the plant reaches maturity, typically at a height of up to 2.5 m. The flowers are relatively short and broad, displaying a white coloration with reddish hues [17,18].

The main rhizome of *C. xanthorrhiza* is generally round and egg-shaped, with a relatively large size. Elongated lateral rhizome branches grow from the sides of the main rhizome, typically numbering three to four per plant. These lateral branches are usually younger and lighter in color compared to the parent rhizome. The outer skin of both young and mature rhizomes ranges from dirty yellow to reddish brown. The inner flesh of the rhizome is yellow to deep orange, characterized by a bitter taste and a distinctive, sharp aroma with moderate fragrance [18]. Rhizomes develop underground at an approximate

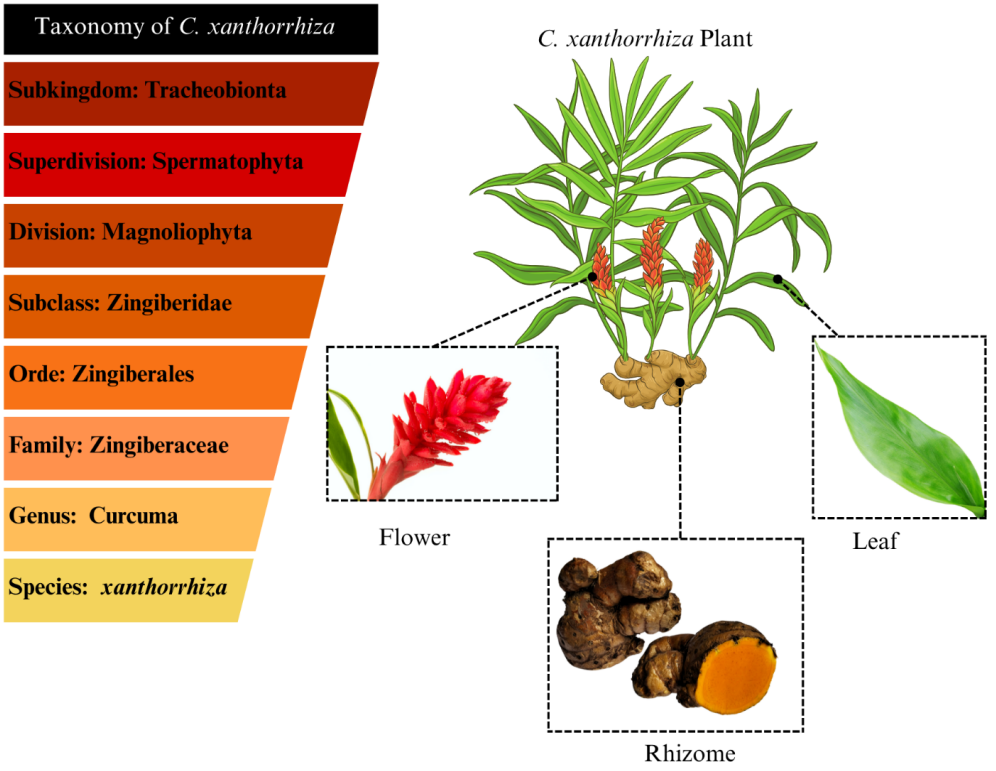


Figure 1. The taxonomic classification and important parts of *C. xanthorrhiza*.

depth of 16 cm. On average, each ginger clump consists of around six mature rhizomes and five younger ones.

Propagation of *C. xanthorrhiza* is typically carried out using rhizome cuttings, either from the main rhizome or from lateral branches. Planting material should be selected from healthy plants aged ten to twelve months, with clean, smooth, shiny skin, and free from pests and diseases. The parent rhizome can be divided into two to four segments, each weighing approximately 20–40 g and containing two–three viable buds. *C. xanthorrhiza* is usually ready for harvest at around ten to twelve months of age. The optimal harvest time is indicated by plant senescence, marked by the drying of stems and leaves.

3. Traditional/ethnomedicinal uses of *C. xanthorrhiza* Roxb.

C. xanthorrhiza has long been utilized by the Indonesian population for various purposes, including as food coloring agent, culinary ingredient, and medicinal remedy. It is commonly used in the preparation of traditional Indonesian herbal drinks, known as *Jamu*, which typically include tamarind, kencur, pandan leaves, and a small amount of palm sugar as a sweetener. In traditional medicine, *C. xanthorrhiza* is valued for its ability to enhance endurance and stamina, as well as for its beneficial effects on digestive health [16,19]. It is used to alleviate stomach-related conditions, such as gastritis (inflammation of the stomach lining), promote the healing of gastric ulcers, prevent stomach cancer, neutralize excess stomach acid, and combat stomach infections. Additionally, *C. xanthorrhiza* is believed to help relieve various digestive complaints, including constipation, nausea, bloating, vomiting, heartburn, and loss of appetite [20,21].

Some medicinal products contain *C. xanthorrhiza* such as Curcuma Plus (PT SOHO Industri Pharmasi, Indonesia), Curcuma (PT SOHO Industri Pharmasi, Indonesia), Sari Temulawak (Sidomuncul), Herbadrink Sari Temulawak, Curcuma

Sanbe (Sanbe Farma), and several other products. Generally, these products have the properties to help maintain healthy liver function and help improve appetite.

The Traditional Herbal Medicine Formulary from the Indonesian Ministry of Health provides guidelines for the proper consumption of *C. xanthorrhiza*. To prepare fresh *temulawak*, 25–50 g of the rhizome is heated in water until it reaches a boil. The resulting boiled water should be consumed 1 h before eating. Alternatively, *temulawak* can be dried and ground into a powder. A recommended dose is 5–15 g of the powdered rhizome, which should be brewed with hot water and consumed while warm [22].

A case study involving Dr Melly Budiman highlights the potential benefits of *temulawak* for liver health. Dr. Melly, who had been diagnosed with liver problems that she suspected were caused by needle transmission, was initially prescribed a high dose of corticosteroids (4 × 10 mg) by her treating physician. However, the treatment was ineffective and resulted in significant side effects, including body swelling. Eventually, Dr. Budiman decided to try consuming boiled *temulawak* water daily for four consecutive months. Upon subsequent biopsy analysis by Dr. Sadikin Darmawan, a senior pathologist, the results indicated that Dr Budiman's liver condition had returned to a healthy state.

4. Phytochemistry

Among the chemicals present in *C. xanthorrhiza*, curcuminoids and terpenoids are the majority, and they possess essential biological properties. The major chemical constituents of *C. xanthorrhiza* are shown in Figure 2.

4.1. *Terpenoids (see Figure 2 for chemical structures)*

Various studies have shown that *C. xanthorrhiza* contains a variety of terpenoids. Septama et al. reported the results of a GC-MS analysis of essential oil extracted from *C. xanthorrhiza*, identifying 42 compounds, primarily consisting of sesquiterpene hydrocarbons (13 compounds): δ-elemene, α-cubebene, copaene, 7-episesquithujene, sesquithujene, *cis*-α-bergamotene, caryophyllene, γ-elemene, β-farnesene, α-curcumene, β-curcumene, β-sesquiphellandrene, germacrene b; oxygenated sesquiterpenes (8 compounds): curzerene, *cis*-sesquisabinene hydrate, β-elemenone, isospathuleno, β-bisabolol, germacrone, curcuphenol, xanthorrhizol; oxygenated monoterpenes (8 compounds): eucalyptol/1,8-cineole, sabinene hydrate, linalool, camphor, isoborneol, borneol, terpinen-4-ol, α-terpineol and monoterpenes (13 compounds): tricyclene, α-pinene, camphene, sabinene, β-pinene, β-myrcene, α-phellandrene, α-terpinene, p-cymene, limonene, β-ocimene, γ-terpinene, α-terpinolene [23]. The major components of essential oil from *C. xanthorrhiza* are α-curcumene, β-curcumene, camphor, and xanthorrhizol [23,24].

A study by Pramono et al. identified the major chemical constituents of *C. xanthorrhiza* as xanthorrhizol, α-cedrene, ar-curcumene, camphor, and curzerenone [25]. Among these, the three most commonly reported compounds are curcumene, camphor, and xanthorrhizol. This composition differs from the findings of Akarchariya et al., who analyzed *C. xanthorrhiza* originating from Chiang Mai, Thailand. Their study identified α-terpinolene, p-cymen-7-ol, p-cymene, and β-pinene as the main components, with no detection of curcumene or xanthorrhizol [26].

As previously noted, although *C. xanthorrhiza* belongs to the same genus as *C. longa*, its essential oil composition is distinct. *C. xanthorrhiza* is particularly rich in monocyclic sesquiterpenes, especially curcumene and xanthorrhizol. In contrast to *C. longa*, the essential oil of *C. xanthorrhiza* lacks α-turmerone and β-turmerone, but contains xanthorrhizol, which serves as a characteristic marker compound for *C. xanthorrhiza* [27]. However, previous research conducted by Uehara [28] reported the presence of nine sesquiterpenoids, including ar-turmerone, α-turmerone, β-turmerone [28].

4.2. *Curcuminoids (see Figure 3 for chemical structures)*

Curcuminoids are linear diarylheptanoid compounds comprising curcumin and its structural analogs. The primary curcuminoids include curcumin, monodemethoxycurcumin, bisdemethoxycurcumin, 1-(4 hydroxy-3,5-dimethoxyphenyl)-7-(4-hydroxy-3-methoxyphenyl)-(1E,6E)-1,6-heptadiene-

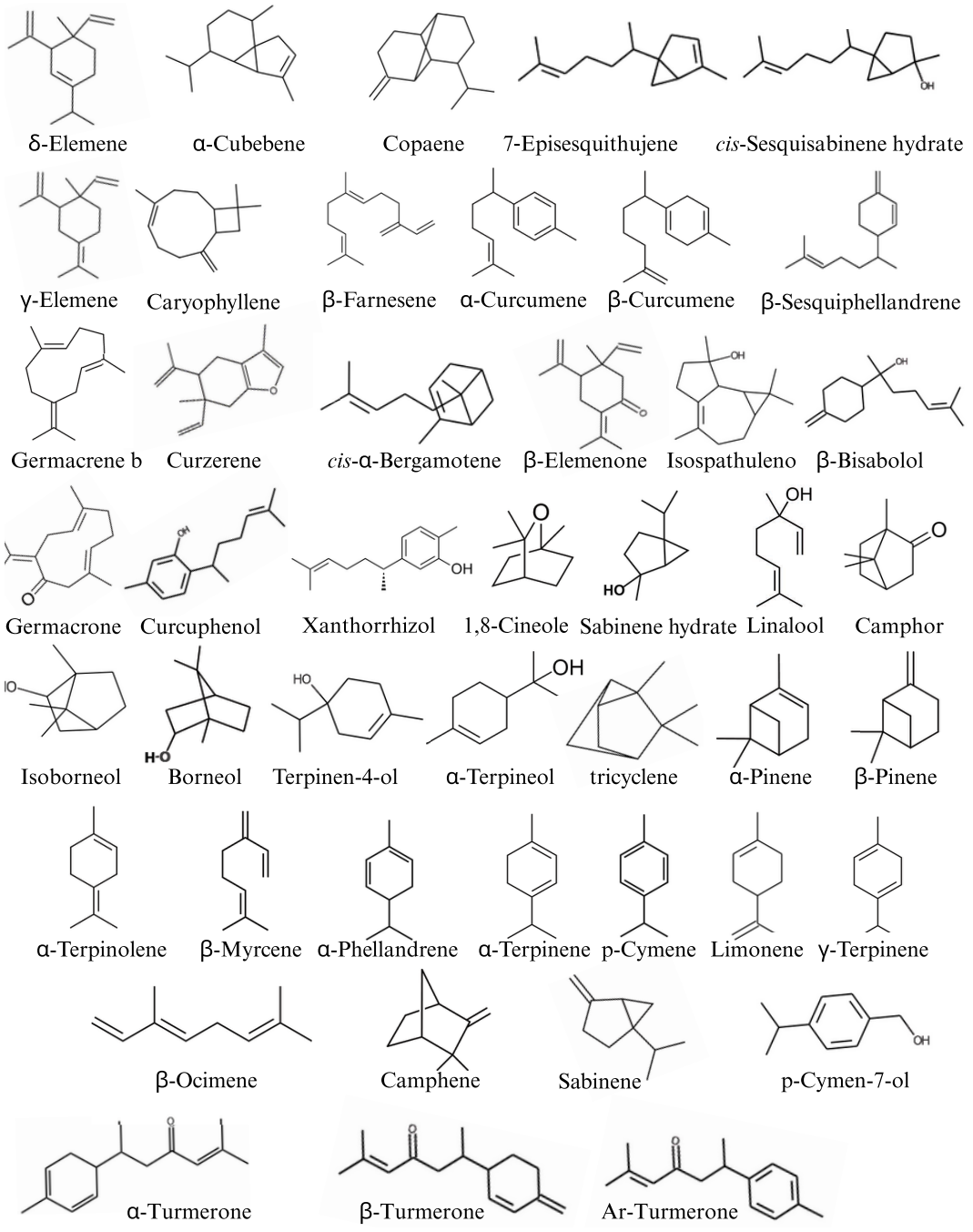


Figure 2. Chemical structures of terpenoids present in *C. xanthorrhiza*.

3,4-dione, dihydrocurcumin, and hexahydrocurcumin [11,29,30]. Erpina [31] identified demethoxycurcumin and bisdemethoxycurcumin in *C. xanthorrhiza*, noting that the concentration of demethoxycurcumin exceeded that of bisdemethoxycurcumin [31].

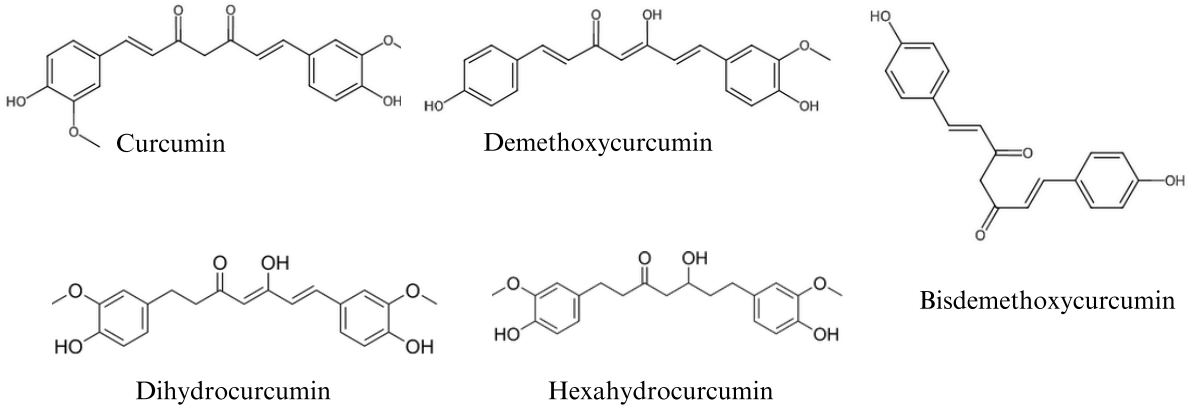


Figure 3. Chemical structure of curcuminoids present in *C. xanthorrhiza*.

5. Hepatoprotective activity

Hepatoprotection refers to the protection of the liver's vital functions—a critical organ central to most physiological processes—through pharmacological or other interventions [32]. It involves the use of chemical agents to restore normal levels of catalase, glutathione peroxidase, and superoxide dismutase activity, thereby safeguarding liver integrity [33]. This hepatoprotective effect is attributed to the presence of antioxidant compounds and their capacity to suppress proinflammatory cytokine activation. Liver injury often arises from dysfunction of essential cellular organelles, triggering excessive reactive oxygen species (ROS) production and subsequent intracellular oxidative stress. ROS-derived free radicals and lipid peroxidation products are key contributors to the pathogenesis of liver fibrosis, hepatocyte necrosis, and hepatic damage [34,35].

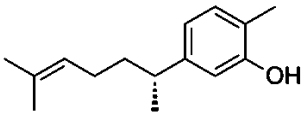
Pretreatment with *C. xanthorrhiza* prior to liver injury demonstrated significant improvement in hepatic biochemical parameters. This was evidenced by reduced serum levels of liver enzymes, including alanine transaminase (ALT), aspartate transaminase (AST), alkaline phosphatase (ALP), serum glutamic-oxaloacetic transaminase (SGOT), and serum glutamic-pyruvic transaminase (SGPT), collectively contributing to its hepatoprotective activity [36]. Furthermore, *C. xanthorrhiza* administration enhanced hepatic antioxidant defenses through elevated activity of superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GPx). This was accompanied by a reduction in lipid peroxidation, as indicated by decreased malondialdehyde (MDA) levels, and promoted histological recovery of liver tissue.

Li et al. [37] examined the dose-dependent hepatoprotective effects of *Curcuma xanthorrhiza* against acute hepatotoxicity induced by D-galactosamine (288 mg/kg, intraperitoneal [i.p.]) in rats, along with its underlying mechanism of action. Following experimental protocols, *C. xanthorrhiza* extract (100 mg/kg) was administered orally (p.o.) prior to a single i.p. dose of hepatotoxin. The results demonstrated that *C. xanthorrhiza* treatment significantly attenuated the acute elevation of serum transaminases induced by hepatotoxin exposure and markedly reduced the severity of hepatic damage observed 24 h post-hepatotoxin administration.

Devaraj et al. [38] conducted a hepatoprotective study on carbon tetrachloride (CCl_4)-induced liver damage in rats using hexane fractions at doses of 125, 250, and 500 mg/kg. The hexane fraction of *C. xanthorrhiza* exhibited the highest antioxidant activity. Regarding hepatoprotective effects, the hexane fraction of *C. xanthorrhiza* demonstrated significant improvements in biochemical liver function markers, antioxidant enzyme levels, and lipid peroxidation activity. Histological analysis also revealed notable recovery in the liver tissues of treated animals.

5.1. *Xanthorrhizol*

Xanthorrhizol is a bisabolane-type sesquiterpenoid compound (Figure 4) extracted from *Curcuma xanthorrhiza* Roxb. This compound has been shown



Xanthorrhizol

Figure 4. Chemical structure of xanthorrhizol.

to exhibit various biological activities, such as anticancer, antimicrobial, anti-inflammatory, antioxidant, antihyperglycemic, antihypertensive, antiplatelet, nephroprotective, hepatoprotective, estrogenic, and antiestrogenic effects. These activities may be attributed to its antioxidant properties and its ability to modulate the expression and activity of key inflammatory mediators, including proinflammatory cytokines [interleukin (IL)-1β, IL-6, tumor necrosis factor-α, matrix metalloproteinases], mediators (cyclooxygenase-2 and inducible nitric oxide synthase), transcription factors (nuclear factor-kappa B [NF-κB] and nuclear factor of activated T cells c1), as well as to regulate diverse signaling pathways involved in inflammation [36,39].

The hepatoprotective effect of xanthorrhizol was evaluated in male ICR (CD-1) mice treated with cisplatin. Cisplatin is a widely used anticancer drug; however, at high doses, it can cause undesirable side effects such as hepatotoxicity.

The mechanism of protection by xanthorrhizol against cisplatin-induced hepatotoxicity was reported by Hong et al. [40] Pretreatment with xanthorrhizol in the liver was associated with the regulation of c-Jun N-terminal kinase (JNK) phosphorylation. Cisplatin-induced JNK phosphorylation, particularly JNK1, was significantly attenuated by xanthorrhizol pretreatment. This finding suggests that JNK phosphorylation may be involved in the protective effect of xanthorrhizol against cisplatin-induced hepatotoxicity and may also influence gene transcription by partially modulating the expression of transcription factor subunits such as c-Fos and p50.

Although studies on the hepatoprotective activity of xanthorrhizol are far more limited compared to curcumin, existing evidence suggests that xanthorrhizol exerts superior suppressive effects against cisplatin-induced nephrotoxicity and hepatotoxicity. At equivalent doses, curcumin demonstrates reduced efficacy in attenuating the elevation of blood urea nitrogen and serum creatinine levels [39]. Molecular pathways in inflammation modulated by xanthorrizol are shown in Figure 5.

5.2. *Curcumin derivatives (curcuminoids)*

The primary curcuminoids that have biological activities include curcumin, demethoxycurcumin, bisdemethoxycurcumin (chemical structures in Figure 6). Curcumin is a hydrophobic polyphenol derived from the rhizome of *Curcuma* species. This compound exhibits diverse pharmacological properties, including anti-inflammatory, antioxidative, antinociceptive, antiparasitic, and antimalarial effects, as well as wound-healing activity [41]. Current research extensively discusses its health benefits, particularly its protective and preventive effects against cancers, diabetes, and various disorders of the liver, nervous system, and cardiovascular systems, while elucidating potential molecular mechanisms. The hepatoprotective effects of curcumin are mediated through multiple pharmacological actions, most notably its potent antioxidant, anti-inflammatory, antifibrotic, and hypolipidemic activities [42,43].

The molecular mechanism of curcumin's hepatoprotective action is mediated through its antioxidant properties and inhibitory activity against nuclear factor (NF)-κB, which regulates various proinflammatory and profibrotic cytokines [44]. Collectively, scientific evidence demonstrates that curcumin possesses significant therapeutic potential for treating liver disorders [45]. Curcumin was identified as a potent inhibitor of rat liver P450 1A1/1A2, measured as ethoxyresorufin-O-deethylase (EROD) activity in β-naphthoflavone (β-NF)-induced microsomes. Curcumin strongly inhibited glutathione S-transferase (GST) activity in the cytosol of rat liver treated with phenobarbital (PB), β-naphthoflavone (β-NF), and pyrazole (Pyr), using 1-chloro-2,4-dinitrobenzene (CDNB) as the substrate [46].

Curcumin demonstrates inhibitory effects on hepatic lipid accumulation. Male ICR (CD-1) mice were fed a bisphenol A (BPA)-contaminated diet supplemented with or without curcumin for 24 weeks. Curcumin supplementation significantly ameliorated BPA-induced hepatic fat accumulation and liver steatosis [47]. Curcumin inhibits platinum-induced hepatic stellate cell activation by downregulating

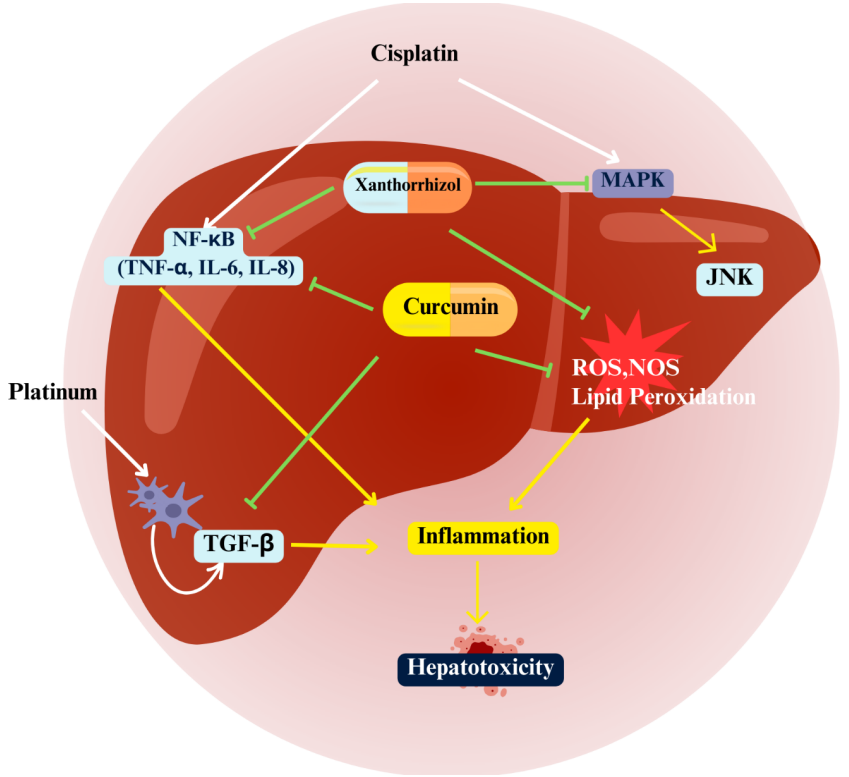


Figure 5. Molecular pathways in inflammation modulated by xanthorrizol and curcumin.

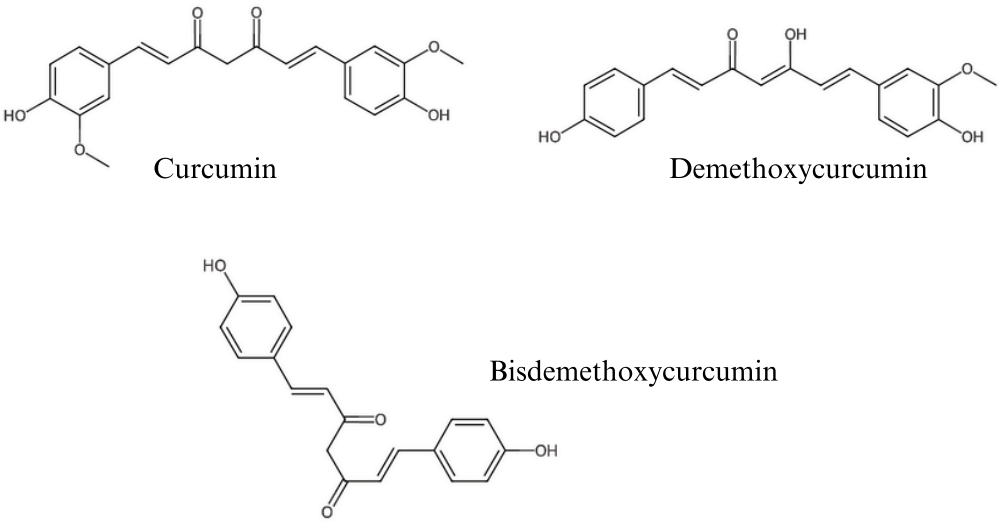


Figure 6. Chemical structure of curcumin derivatives.

transforming growth factor-beta (TGF-β) signaling and suppressing collagen synthesis, thereby preventing liver fibrosis progression and preserving hepatic architecture [48]. Oral administration of curcumin (300 mg/kg) attenuates liver fibrosis in BALB/c mice by inhibiting hepatic stellate cell activation and inducing apoptosis of damaged hepatocytes [49].

Terpene-conjugated curcumin (TCC) was evaluated in an alcoholic liver disease (ALD) model using 8-week-old male Sprague-Dawley rats. TCC treatment significantly improved liver function, reduced lipid accumulation, and alleviated inflammation compared to the model group. Mechanistically, TCC inhibited the TLR4/MyD88/NF-κB signaling pathway, decreased endotoxin translocation, enhanced intestinal tight junction protein expression, and promoted secretory IgA (sIgA) production [50]. Curcumin enhances autophagy (increasing LC3-II gene expression and decreasing sequestosome 1 (SQSTM1) concentration) while inhibiting apoptosis (upregulating Bcl-2 gene expression). High-dose curcumin provides superior protection against liver fibrosis by significantly reducing ALT, AST, and ALP levels, as well as lipid peroxidation. Furthermore, curcumin pretreatment increased hepatic heme oxygenase 1 (HO-1) expression by 2.4-fold while reducing nitric oxide synthase 2 (NOS-2) expression by 4.1-fold [51].

In vitro, 50 μM curcumin significantly reduced HepG2 cell viability and SQSTM1 concentration. These findings suggest that curcumin and other autophagy activators may be potentially useful for protection against early-stage hepatocellular carcinoma (HCC) [52]. In another study, curcumin administration prevented liver damage induced by a cadmium–arsenic mixture. Curcumin treatment significantly reduced inflammation, oxidative stress, and lipid peroxidation in mice receiving both cadmium–arsenic and curcumin compared to those receiving cadmium–arsenic alone. Furthermore, histological examination of liver tissue revealed that curcumin treatment resulted in a significant reduction of liver damage observed in the cadmium–arsenic-exposed group [53]. Molecular pathways in inflammation modulated by curcumin are shown in Figure 5.

Demethoxycurcumin and bisdemethoxycurcumin are curcuminoid compounds other than curcumin. These two compounds have been less studied and reported in the literature regarding their bioactivity. Demethoxycurcumin and bisdemethoxycurcumin exhibit antioxidant activity with IC_{50} values of 12.46 and 17.94 μg/mL, respectively. Meanwhile, bisdemethoxycurcumin demonstrates a better IC50 value than demethoxycurcumin against the HepG2 cell line (64.7 μM) [54]. In other studies, in vitro models, such as the phosphomolybdenum peroxidation and linoleic acid methods, were used. The antioxidant capacity of the extract, expressed as ascorbic acid equivalents (μmol/g) and butylated hydroxytoluene (BHT), at 100 ppm, revealed antioxidant activity in the following order (via linoleic acid peroxidation): curcumin > demethoxycurcumin > bisdemethoxycurcumin. The reported results demonstrate the antioxidant potential of each curcuminoid [55].

Lee et al. [56] demonstrated through in vivo studies using C57BL/6J mouse models that administration of curcumin, demethoxycurcumin, and bisdemethoxycurcumin significantly reduced methionine-choline diet-induced lipid accumulation and elevated levels of triglyceride (TG) and total cholesterol (TC). These three curcuminoids exhibited hepatoprotective effects in both HepG2 cell models and methionine-choline diet-induced non-alcoholic fatty liver disease (NAFLD) models. Cheon [57] investigated the protective activity of curcumin, demethoxycurcumin, and bisdemethoxycurcumin against hepatocyte injury induced by carbon tetrachloride (CCl_4, 10 mM), tert-butyl hydroperoxide (TBH, 0.5 mM), and D-galactosamine (GalN, 30 mM). Curcumin and bisdemethoxycurcumin exhibited strong hepatoprotective activity. Curcumin inhibited the CCl_4-induced increase in lactate dehydrogenase (LDH), alanine aminotransferase (ALT), and aspartate aminotransferase (AST) levels. In TBH-induced injury, curcumin suppressed the elevation of ALT and AST, while bisdemethoxycurcumin inhibited the increase in LDH, ALT, and AST levels. For GalN-induced injury, the rise in LDH, ALT, and AST levels was significantly suppressed by bisdemethoxycurcumin.

6. Conclusion

C. xanthorrhiza has been traditionally used for generations. Both traditional medicinal practices and

scientific studies indicate its hepatoprotective properties against liver damage. Active compounds such as xanthorrhizol and curcuminoids (including curcumin and bisdemethoxycurcumin) are strongly suggested to mediate these protective effects. However, despite its widespread use, further research is still required to fully understand the potential side effects associated with *C. xanthorrhiza* consumption.

Declaration of interests

The authors do not work for, advise, own shares in, or receive funds from any organization that could benefit from this article, and have declared no affiliations other than their research organizations.

References

[1] C. Gan, Y. Yuan, H. Shen, J. Gao, X. Kong, Z. Che, Y. Guo and H. Wang, "Liver diseases: epidemiology, causes, trends and predictions", *Signal Transduct. Target. Ther.* **10** (2025), article no. 33.

[2] H. Wazir, M. Abid, B. Essani, et al., "Diagnosis and treatment of liver disease: current trends and future directions", *Cureus* **15** (2023), no. 12, article no. e49920.

[3] Z. Nouri, S. Fakhri, K. Nouri, C. E. Wallace, M. H. Farzaei and A. Bishayee, "Targeting multiple signaling pathways in cancer: the rutin therapeutic approach", *Cancers* **12** (2020), no. 8, pp. 1–34.

[4] H. Y. K. Yip and A. Papa, "Signaling pathways in cancer: therapeutic targets, combinatorial treatments, and new developments", *Cells* **10** (2021), no. 3, pp. 1–30.

[5] M. You, Z. Xie, N. Zhang, et al., "Signaling pathways in cancer metabolism: mechanisms and therapeutic targets", *Signal Transduct. Target. Ther.* **8** (2023), no. 1, pp. 1–27.

[6] M. B. Lustberg, N. M. Kuderer, A. Desai, C. Bergerot and G. H. Lyman, "Mitigating long-term and delayed adverse events associated with cancer treatment: implications for survivorship", *Nat. Rev. Clin. Oncol.* **20** (2023), no. 8, pp. 527–542.

[7] U. Anand, A. Dey, A. K. S. Chandel, et al., "Cancer chemotherapy and beyond: Current status, drug candidates, associated risks and progress in targeted therapeutics", *Genes Dis.* **10** (2023), no. 4, pp. 1367–1401.

[8] J. L. Raoul, M. Gilabert and G. Piana, "How to define transarterial chemoembolization failure or refractoriness: a European perspective", *Liver Cancer* **3** (2014), no. 2, pp. 119–124.

[9] N. S. Dosoky and W. N. Setzer, "Chemical composition and biological activities of essential oils of curcuma species", *Nutrients* **10** (2018), no. 9, pp. 10–17.

[10] T. Estiasih, J. M. Maligan, J. E. Witoyo, A. A. H. Mu'alim, K. Ahmadi, T. Mahatmanto and E. Zubaidah, "Indonesian traditional herbal drinks: diversity, processing, and health benefits", *J. Ethn. Food* **12** (2025), no. 7, pp. 4–8.

[11] E. Rahmat, J. Lee and Y. Kang, "Javanese turmeric (Curcuma xanthorrhiza Roxb.): ethnobotany, phytochemistry, biotechnology, and pharmacological activities", *Evidence-based Complement. Altern. Med.* **2021** (2021), pp. 1–15.

[12] H. Kim, D. W. Lee and J. K. Hwang, "Curcuma xanthorrhiza extract and xanthorrhizol ameliorate cancer-induced adipose wasting in CT26-bearing mice by regulating lipid metabolism and adipose tissue browning", *Integr. Med. Res.* **13** (2024), no. 1, pp. 1–7.

[13] M. E. Klau, E. Rohaeti, M. Rafi, I. M. Artika, L. Ambarsari and W. Nurcholis, "Metabolite profiling of curcuma zanthorrhiza varieties grown in different regions using UHPLC-Q-Orbitrap-HRMS and chemometrics analysis", *Biointerf. Res. Appl. Chem.* **13** (2023), no. 1, pp. 1–13.

[14] J. Mishra, A. Bhardwaj and K. Misra, "*Curcuma* sp.: the nature's souvenir for high-altitude illness", in *Management of High Altitude Pathophysiology* (K. Misra, P. Sharma and A. Bhardwaj, eds.), Elsevier Inc.: Amsterdam, 2018, pp. 153–169.

[15] S. Fuloria, J. Mehta, A. Chandel, et al., "A comprehensive review on the therapeutic potential of Curcuma longa Linn. in relation to its major active constituent curcumin", *Front. Pharmacol.* **13** (2022), no. March, pp. 1–27.

[16] R. A. M. R. Syamsudin, F. Perdana, F. Suci Mutiaz, et al., "Temulawak plant (Curcuma xanthorrhiza Roxb) as a traditional medicine", *J. Ilm. Farm. Bahari* **10** (2019), no. 1, pp. 51–65.

[17] D. Suniarti, R. Puspitawati, R. Yanuar and R. Herdiantoputri, "*Curcuma Xanthorrhiza* Roxb. An indonesia native medicinal plant with potential antioral biofilm effect", in *Focus on Bacterial Biofilms*, Intech Open: London, 2022, pp. 1–16.

[18] M. Silalahi, N. Nisyawati, E. C. Purba and D. W. Abinawanto, "Ethnobotanical study of zingiberaceae rhizomes as traditional medicine ingredients by medicinal plant traders in the Pancur Batu traditional market, The Ethnobiological Society of Indonesia", *J. Trop. Ethno.* **4** (2021), no. 2, pp. 78–95.

[19] Ministry of Health Republic Indonesia, *Formularium Ramuan Obat Tradisional Indonesia (FROTI)*, Kementerian Kesehatan RI: Jakarta, 2020.

[20] N. A. Rahim, P. Hassandarvish, S. Golbabapour, S. Ismail, S. Tayyab and M. A. Abdulla, "Gastroprotective effect of ethanolic extract of Curcuma xanthorrhiza leaf against ethanol-induced gastric mucosal lesions in sprague-dawley rats", *Biomed Res. Int.* **2014** (2014), article no. 416409.

[21] N. Hakim and A. Z. Wakhidah, "Ethnobotany of medicinal plants from Lampung Tribe around Way Kambas National Park, Indonesia", *Nusantara Biosci.* **14** (2022), no. 1, pp. 84–94.

[22] Ministry of Health Republic Indonesia, *Formularium Ramuan Obat Tradisional Indonesia (FROTI)*, Kementerian Kesehatan RI: Jakarta, 2021.

[23] A. W. Septama, A. N. Tasfiyati, R. Kristiana and A. Jaisi, "Chemical profiles of essential oil from Javanese turmeric (Curcuma xanthorrhiza Roxb.), evaluation of its antibacterial and antibiofilm activities against selected clinical isolates", *South African J. Bot.* **146** (2022), pp. 728–734.

[24] C. A. Rahman, L. M. Rahmawati, D. Santosa, P. Indrasetiawan and Purwanto, "Essential Oil Profiling and Antibacterial Activity of Curcuma xanthorrhiza Roxb. Originated from Yogyakarta by GC-MS", *Maj. Obat Tradis.* **29** (2024), no. 2, pp. 223–232.

[25] S. Pramono, F. H. Arifah, F. H. Pribadi and A. E. Nugroho, "Hepatoprotective activity of curcuma xanthorrhiza Roxb. On paracetamol-induced liver damage in rats and correlation with their chemical compounds", *Thai J. Pharm. Sci.s* **42** (2018), no. 4, pp. 188–195.

[26] N. Akarchariya, S. Sirilun, J. Julsrigival and S. Chansakaowa, "Chemical profiling and antimicrobial activity of essential oil from Curcuma aeruginosa Roxb., Curcuma glans K. Larsen and J. Mood and Curcuma cf. xanthorrhiza Roxb. collected in Thailand", *Asian Pac. J. Trop. Biomed.* **7** (2017), no. 10, pp. 881–885.

[27] K. Losso, K. B. Bec, S. Mayr, et al., "Rapid discrimination of Curcuma longa and Curcuma xanthorrhiza using direct analysis in real time mass spectrometry and near infrared spectroscopy", *Spectrochim. Acta* **265** (2022), article no. 120347.

[28] S. Uehara, I. Yasuda, K. Takeya and H. Itokawa, "Terpenoids and curcuminoids of the rhizoma of Curcuma xanthorrhiza Roxb", *Yakugaku Zasshi* **112** (1992), no. 11, pp. 817–823.

[29] M. Lechtenberg, B. Quandt and A. Nahrstedt, "Quantitative determination of curcuminoids in Curcuma rhizomes and rapid differentiation of Curcuma domestica Val. and Curcuma xanthorrhiza Roxb. by capillary electrophoresis", *Phytochem. Anal.* **15** (2004), no. 3, pp. 152–158.

[30] J. H. Park, Y. J. Jung, S. Shrestha, et al., "Inhibition of NO production in LPS-stimulated RAW264.7 macrophage cells with curcuminoids and xanthorrhizol from the rhizome of Curcuma xanthorrhiza Roxb. and quantitative analysis using HPLC", *J. Korean Soc. Appl. Biol. Chem.* **57** (2014), pp. 407–412.

[31] E. Erpina, M. Rafi, L. K. Darusman, A. Vitasari, B. R. Putra and E. Rohaeti, "Simultaneous quantification of curcuminoids and xanthorrhizol in Curcuma xanthorrhiza by high-performance liquid chromatography", *J. Liq. Chromatogr. Relat. Technol.* **40** (2017), no. 12, pp. 635–639.

[32] M. Y. Alkandahri, B. T. Pamungkas, Z. Oktoba, et al., "Hepatoprotective effect of kaempferol: a review of the dietary sources, bioavailability, mechanisms of action, and safety", *Adv. Pharmacol. Pharm. Sci.,* **2023** (2023), article no. 1387665.

[33] A. Bihari, R. Rekha, N. Kumar and A. K. Duttaroy, "Biomedicine and Pharmacotherapy Cellular Red-Ox system in health and disease: The latest update", *Biomed. Pharmacother.* **162** (2023), article no. 114606.

[34] P. Sharma, M. Nandave, D. Nandave, S. Yadav and C. Vargas-de-la-cruz, "Reactive oxygen species (ROS)-mediated oxidative stress in chronic liver diseases and its mitigation by medicinal plants", *Am. J. Transl. Res.* **15** (2023), no. 11, pp. 6321–6341.

[35] R. Gopal, R. Mooli, D. Mukhi and S. K. Ramakrishnan, "Oxidative stress and redox signaling in the pathophysiology of liver diseases", *Compr Physiol.* **12** (2023), no. 2, pp. 3167–3192.

[36] A. Simamora, K. H. Timotius, H. Setiawan, M. B. Yerer, R. A. Ningrum and A. Mun'im, "Xanthorrhizol: its bioactivities and health benefits", *J. Appl. Pharm. Sci.* **14** (2024), no. 2, pp. 27–39.

[37] S. C. Li, C. C. Lin, Y. H. Lin, S. Supriyatna and C. W. Ten, "Protective and therapeutic effects of Curcuma xanthorrhiza on Hepatotoxin-induced liver damage", *Am. J. Chin. Med.* **23** (1996), pp. 13–24.

[38] S. Devaraj, S. Ismail, S. Ramanathan and M. F. Yam, "Investigation of antioxidant and hepatoprotective activity of standardized curcuma xanthorrhiza rhizome in carbon tetrachloride-induced hepatic damaged rats", *Sci. World J.* **2014** (2014), article no. 353128.

[39] S. F. Oon, M. Nallappan, T. T. Tee, S. Shohaimi, N. K. Kassim, M. S. F. Sa'ariwijaya and Y. H. Cheah, "Xanthorrhizol: a review of its pharmacological activities and anticancer properties", *Cancer Cell Int.* **15** (2015), no. 1, pp. 1–15.

[40] K. O. Hong, J. K. Hwang, K.-K. Park and S. H. Kim, "Phosphorylation of c-Jun N-terminal Kinases (JNKs) is involved in the preventive effect of xanthorrhizol on cisplatin-induced hepatotoxicity", *Arch. Toxicol.* **79** (2005), no. 4, pp. 231–236.

[41] V. Ruiz de Porras, M. Figols, A. Font and E. Pardina, "Curcumin as a hepatoprotective agent against chemotherapy-induced liver injury", *Life Sci.* **332** (2023), no. 8, article no. 122119.

[42] M. H. Farzaei, M. Zobeiri, F. Parvizi, et al., "Curcumin in liver diseases: a systematic review of the cellular mechanisms of oxidative stress and clinical perspective", *Nutrients* **10** (2018), no. 7, article no. 855.

[43] M. I. Alam, M. Mohamed, E. Taha, Y. Almoshari and S. S. Alqahtani, "Hepatoprotective effect of curcumin nanolipid carrier inflammatory, and apoptotic changes in wistar rats", *Molecules* **28** (2023), article no. 881.

[44] M. R. Islam, A. Rauf, S. Akash, et al., "Targeted therapies of curcumin focus on its therapeutic benefits in cancers and human health: molecular signaling pathway-based approaches and future perspectives", *Biomed. Pharmacother.* **170** (2024), article no. 116034.

[45] S. F. Nabavi, M. Daglia, A. H. Moghaddam, S. Habtemariam and S. M. Nabavi, "Curcumin and liver disease: from chemistry to medicine", *Compr. Rev. Food Sci. Food Saf.* **13** (2014), no. 1, pp. 62–77.

[46] S. Oetari, M. Sudibyo, J. N. M. Commandeur, R. Samhoedi and N. P. E. Vermeulen, "Effects of curcumin on cytochrome P450 and glutathione S-transferase activities in rat liver", *Biochem. Pharmacol.* **51** (1996), no. 1, pp. 1–9.

[47] T. Hong, X. Jiang, J. Zou, J. Yang, H. Zhang, H. Mai, W. Lin and D. Feng, "Hepatoprotective effect of curcumin against bisphenol A-induced hepatic steatosis via modulating gut microbiota dysbiosis and related gut-liver axis activation in CD-1 mice", *J. Nutr. Biochem.* **109** (2022), article no. 109103.

[48] X. Peng, C. Dai, Q. Liu, J. Li and J. Qiu, "Curcumin attenuates on carbon tetrachloride-induced acute liver injury in mice via modulation of the Nrf2/HO-1 and TGF-β1/Smad3 pathway", *Molecules* **23** (2018), no. 1, pp. 1–16.

[49] M. E. Wang, Y. C. Chen, I. S. Chen, S. C. Hsieh, S. S. Chen and C. H. Chiu, "Curcumin protects against

thioacetamide-induced hepatic fibrosis by attenuating the inflammatory response and inducing apoptosis of damaged hepatocytes", *J. Nutr. Biochem.* **23** (2012), no. 10, pp. 1352–1366.

[50] S. Tao, S. Ruanping, Z. Wang, et al., "Terpene-conjugated curcumin analogs alleviated alcoholic liver injury in rats through mitigation of intestinal barrier abnormalities", *Food Biosci.* **68** (2025), article no. 106532.

[51] D. Černý, L. Nataša, K. Váňová, et al., "Hepatoprotective effect of curcumin in lipopolysaccharide/-galactosamine model of liver injury in rats: Relationship to HO-1/CO antioxidant system", *Fitoterapia* **82** (2011), no. 5, pp. 786–791.

[52] A. M. Elmansi, A. A. El-Karef, M. M. El-Shishtawy and L. A. Eissa, "Hepatoprotective effect of curcumin on hepatocellular carcinoma through autophagic and apoptic pathways", *Ann. Hepatol.* **16** (2017), no. 4, pp. 607–618.

[53] M. C. B. Gür, C. V. Sezer, B. P. Cengiz, F. Gür, A. Bayrakdar and A. Ayhancı, "Alternations in interleukin-1β and nuclear factor kappa beta activity (NF-kB) in rat liver due to the co-exposure of Cadmium and Arsenic: Protective role of curcumin", *Environ. Toxicol. Pharmacol.* **102** (2023), article no. 104218.

[54] A. M. Araya-Sibaja, F. Vargas-Huertas, S. Quesada, G. Azofeifa, J. R. Vega-Baudrit and M. Navarro-Hoyos, "Characterization, antioxidant and Cytotoxic evaluation of demethoxycurcumin and bisdemethoxycurcumin from Curcuma longa cultivated in Costa Rica", *Separations* **11** (2024), no. 1, pp. 1–16.

[55] G. K. Jayaprakasha, L. J. Rao and K. K. Sakariah, "Antioxidant activities of curcumin, demethoxycurcumin and bisdemethoxycurcumin", *Food Chem.* **98** (2008), pp. 720–724.

[56] Y. S. Lee, S. M. Oh, Q. Q. Li, et al., "Validation of a quantification method for curcumin derivatives and their hepatoprotective effects on nonalcoholic fatty liver disease", *Curr. Issues Mol. Biol.* **44** (2022), no. 1, pp. 409–432.

[57] H. J. Cheon, J. G. Park, K. Sun-young, S. S. Kang, X. Cai, J. Lee and S. Lee, "Hepatoprotective activities of curcumin, demethoxycurcumin and bisdemethoxycurcumin", *Korean J. Pharmacogn.* **38** (2007), no. 2, pp. 139–147.