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Review Article

A Comprehensive Study on the Cytotoxic Action of Bioactive Compounds of Three Himalayan Herbs

Gaurav Upadhyay*, Rajesh Kumar Sharma

Department of Pharmacognosy, Teerthanker Mahaveer College of Pharmacy, Teerthanker Mahaveer University, NH-9, Delhi Road, Moradabad, Uttar Pradesh, INDIA.

ABSTRACT

Globally, Hepatocellular Carcinoma (HCC) is one of the main causes of cancer-related mortality generally affecting men more than women, and with an age of onset between late teens and 30s. Lamiaceae family also known as mint family containing aromatic flowering herbs. The potential of herbs in the Lamiaceae family, especially those indigenous to the Himalayan region has been brought to light by recent developments against HCC. Three such Himalayan herbs-Buggleweed (*Ajuga bracteosa* Wall. ex Benth), Wild marjoram (*Origanum vulgare* Linn.) and Ashy Roylea (*Roylea elegans* Wall.) along with their bioactive substances have cytotoxic effects on HCC are the subject of this review. These herbs are well-known for their abundant phytochemical makeup, which includes Essential Oils (EO's), diterpenoids. phenolic acids, and flavonoids having strong anti-cancer properties. These include the capacity to regulate important cellular functions including apoptosis, cell cycle regulation, and angiogenesis, as well as antioxidant action, which is essential for preventing DNA damage brought on by oxidative stress. These herbs are very appealing for the prevention and treatment of HCC because of their capacity to increase the activity of liver detoxifying enzymes and guard against liver fibrosis. These plants are a great source of possible therapeutic agents for the prevention and treatment of hepatocellular carcinoma because of their widespread availability and diverse chemical makeup. Incorporating these plant-based substances into existing treatment plans may offer a more comprehensive and economical strategy for battling this debilitating illness.

Keywords: Hepatocellular carcinoma, Himalayan herbs, Lamiaceae family, Cytotoxic action, Bioactive compounds, Therapeutic potential, Apoptosis.

Correspondence:
Gaurav Upadhyay
Department of Pharmacognosy, Research Scholar, Teerthanker Mahaveer College of Pharmacy, Teerthanker Mahaveer University, NH-9, Delhi Road, Moradabad, Uttar Pradesh, INDIA.
Email: constantine.upadhyay23@gmail.com

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INTRODUCTION

Botanicals and their extracts employed from thousands of years as folk medicines used in several diseases and ailments. Lamiaceae family is the family of flowering plants containing aromatic herbs, shrubs and few trees is considered as sixth largest family having more than 7000 species with 250 genera. This family also known as 'Mint family' comprising large number of Essential Oils (EO's) and their components. Formerly, it was named as Labiatae under International Code of Nomenclature for algae, fungi, and plants (Melbourne Code) and also named as deadnettle, sage, irumba-hare, Chun xing ke, lumbase nilcols or irumbahe in some areas of Asian countries.[1] Some of the important genera in this family are Salvia, Thymus, Vitex, Mentha, Ocimum, Lavandula, Melissa, Scutellaria, Stachys etc. They are used in traditional remedies in the treatment of various ailments such as inflammation, gastritis, dermatitis, infections, bronchitis etc. and many more. The EO's are found in all most all parts of plants store in epidermic cells, secretory cells, canals, cavities, canals or glandular trichomes. These are mainly composed of monoterpenes and sesquiterpenes hydrocarbons, phenylpropanoids and rarely di and tetra terpenes.[2] The scientific interest has become popular because of their wide range of pharmacological activities and act as synergistically with other shows promising action as antimicrobial, cytotoxic, anti-diabetic, anti-inflammatory, antimycotic and antimutagenic properties.

Hepatocellular Carcinoma (HCC) is the fourth most common cause of cancer-related death worldwide generally affecting men more than women, and with an age of onset between late teens and 30s. In India, about 45 million people suffering from chronic Hepatitis B Virus (HBV) infection and approximately 15 million people are afflicted with chronic Hepatitis C Virus (HCV) infection. Both HBV and HCV are considered as important etiologic factors in HCC.[3] It is also associated with impaired liver function generally caused due to the exposure of drug/chemicals or another non-infectious agent. The causes are may be predictable or unpredictable; predictable causes are typically dose related and occurs in the short exposure of any drug on/after its threshold for

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toxicity. Some chemicals such as CCl_4, phosphorus, chloroform etc. are unpredictable hepatotoxins, dose independent and have variable latency period at the time of onset.[4] Additionally, Risk factors of HCC are high in alcohol addiction, metabolic liver disease (particularly non-alcoholic fatty liver disease) and exposure to dietary toxins such as aflatoxins and aristolochic acid.[5] However, there is no defined curative treatment of HCC and associated liver diseases. Only palliative treatments such as surgical resection, chemoembolization, liver transplantation etc., may be considered as option. There are numerous side effects of modern allopathic medications for treatment of hepatotoxicity and other liver diseases.

Recently, the Essential Oils (EOs) from lamiaceae plant species and their extracts have been studied for their promising action towards treatment in various types of cancer involving their cytotoxic action towards apoptosis and cell cycle arrest. They have been also screened for anti-tumor potential by inhibiting the metastasis cycle and acts as anti-multidrug resistance of compounds used in different types of cancer.[6]

METHODOLOGY

To explore more research on selected herbs associated with Lamiaceae family for preventing and controlling the HCC, A literature review was conducted using different scientific databases such as Scopus, PubMed, Elsevier, Embase and Google Scholar. The purpose of review to explore relevant data of selected Lamiaceae species in chemo protective action against HCC along with mechanism of action. The review also helps researchers to explore chemical purification and chromatographic analysis of plants for investigation of more chemical content as mentioned in Table 1.

SELECTED HERBS

Ajuga bracteosa Wall. ex Benth

Ajuga bracteosa Wall. ex Benth commonly known as Buggleweed or Neelkanthi is widely distributed in Himalayan region at an altitude of 1220-3000 m (Figure 1). It is commonly found in Grassy hillsides, roadsides, weed of paddy-fields and also cultivated in many regions of Uttarakhand and Himanchal due its large variety of medicinal properties.[13,14] It is an evergreen clump-forming flowering plant grows up to the height of 5-50 cm with purplish-green stalked leaves arranged in opposite pairs.[15] The leaves are elliptical or ovate with rounded tip, hairless with dentate margin.

The flowers are short and flat with a smooth edge, 14 to 17 mm (0.6 to 0.7 in) long with a short tube, blue colour with dark veins on the lower lip. The inflorescence consists of dense raceme calyx, five toothed lobed corollas containing four stamens longer than petals attached to the centre of tube. The stems are runners that spread across the surface of the ground, square shaped in cross-section with hairs on two sides.[16] The whole plant contains various phyto-constitutions like essential oils as neo-clerodane diterpenoids, steroids, flavonoids, fatty acids, iridoids, triglycerides, withanolides, phenylethanoid glycosides and quinols. The leaves contain essential oils such as Limonene, α-humulene, β- Myrcene, Elemol, Camphene, β-Caryophellene and α –phellandrene.[17] The whole plant is used as remedy for fever, dysentery, diabetes, malaria, toothache, high blood pressure, gastrointestinal disorders etc. It is also used in the treatment of gout and rheumatism, astringent, aperient, stimulant, diuretic etc. The whole plant is used as powerful remedy for burns and boils. The Juice of the leaves is used as blood purifier.[18]

Different biological activities related to antioxidant and cytotoxic action of *Ajuga bracteosa*

Vohra and Kaur (2011)[19] reported the essential oils from leaves of *Ajuga bracteosa* and screened their antibacterial potential different bacterial strain as *E. coli, Bacillus, Pseudomonas* and *Staphylococcus*. The main components of essential oils were found as Limonene, β-Myrcene, α-humulene Elemol, β-Caryophellene, Camphene and α-phellandrene. These oils were analyzed by GC-MS and results showed minimum inhibiting concentration effectively against *E. coli* and *Staphylococcus strains*. Riaz *et al*., (2007)[20] isolated active components of essential oils from whole plant of *Ajuga bracteosa* performed enzyme inhibitory potential against different enzymes as for lipoxygenase, butyryl-cholinesterase and acetyl-cholinesterase. The essential oils characterized by 1D- and 2D-NMR spectroscopy identified as diterpenoids as Bractin A (=(2S,3S,4R,5E)-2-{[(2R)-2-hydroxydodecanoyl]amino} triacont-5-ene-1,3,4-triol; 1), Bractin B (=(2S,3S,4R,5E,8E)-2-{[(2R)-2-hydroxyhexacosanoyl]amino}pentadeca-5,8-diene-3,4,15-triol1-O-β-D lucopyranoside; 2), new sphingolipids and Bractic acid (=(5Z,10Z,15Z)-2-decyl-4,7,8,12,13,17,18-heptahydroxy-20,23-dioxopentacosa-5,10,15-trienoic acid; 3). All isolated compounds showed non-competitive type of inhibition with different Ki values (9.5–35.2, 15.2–36.0, and 11.6–20.5 μM) for different lipoxygenase, acetyl-cholinesterase, and butyryl-cholinesterase, respectively. Singh *et al*., (2006)[21] isolated a new phthalic acid ester (1,2-benzenedicarboxylic acid bis (2S-methyl heptyl) ester) from hexane extract and neo-clerodane diterpene ajugarin-I from chloroform extract and two iridoid glycosides, reptoside and 8-O-acetyl harpagide from methanolic extract of whole plant of *Ajuga bracteosa*. All isolated compounds were analyzed by extensive spectroscopic analysis and volatile oil constituents were identified by GC-MS. Additionally a new source of linalyl acetate, a valuable perfumery compound was also identified. Ahanger and Kumar (2022)[22] developed nanoscale ZIF-8 core encapsulated drug from methanolic extract of *Ajuga bracteosa* by using Zeolitic imidazolate framework-8and reported its cytotoxic effects by inhibition in growth of A549 human caucasian lung carcinoma cell line. Rubnawaz *et al*., (2021)[23] transformed *Ajuga bracteosa*

into transgenic rolB genes of *Agrobacterium rhizogenes* by using hairy roots culture and reported its cytotoxic potential by Brine shrimp assay. Among them, ABRL3 was most effective against cell lines HepG2, LM3, A549, HT29, MCF-7, and MDA-MB-231, respectively. Ganaie *et al*., (2017)[24] isolated four major compounds identified as β- Sitosterol, 14, 15-dihydroajugapitin and 8-O-acetylharpagide from the methanol extract of *Ajuga bracteosa* using silica gel column chromatography. The isolated compounds and standard drug were screened for *in vivo* mutagenic activity against EMS induced mutagenicity model followed by micronucleus and chromosomal aberration tests. Pal *et al*., (2014)[25] isolated β-sitosterol from the methanolic fraction from aerial parts of *Ajuga bracteosa* and studied its cytotoxic effects in Hep-2 and MCF-7 tumor cell lines. The results showed decrease in tumor frequency and tumor volume as compared to control.

Origanum vulgare Linn.

Origanum vulgare Linn. belonging to mint family (Lamiaceae) commonly known as Oregano, Wild marjoram and Winter sweet is a perennial herbaceous plant native to Mediterranean region and Eurasia.[26] In India, its only one species (*Origanum vulgare*) is found in Himalayas at altitude of 1500-3600 known as 'Ban-tulsi' (Figure 2).

The aerial parts of plant contain variety of phytoconstituents such as flavonoids, phenolic compounds, glycosides, sterols, tannins, and high amounts of terpenoids. The essential oil contains active principle as monoterpenoids such as carvacrol, thymol, linalool, and p-cymene[27,28] and also comprising of sesquiterpene hydrocarbons such as α-humulene, β-caryophyllene, spathulenol and germacrene D.[29] Among them, spathulenol is the most abundantly found in aerial parts.[30] The plant is reported two acid ester derivatives named origanol A and origanol B protocatechuic with ursolic acid, β-sitosterol, oleanolic acid and triacontanol from the aerial's parts of plant.[31] Traditionally, whole plant has been reported to have culinary and medicinally purpose. The leaves have beneficial effects on respiratory and digestive system and also promote menstruation.[32] The flowering parts and stem are widely used as carminative, antiseptic, antispasmodic, diaphoretic, cholagogue, expectorant, emmenagogue, stimulant, stomachic, indigestion and mild feverish illnesses and in painful menstruation.[33]

Biological studies related to antioxidant and cytotoxic action of *Origanum vulgare*

Mancini *et al*., (2014)[34] reported *in vitro* phytotoxic activity of essential oils from *Origanum vulgare* ssp. Hirtum in germination and initial radicle elongation of *Phalaris canariensis* L., *Sinapis arvensis* L., *Lepidium sativum* L. and *Raphanus sativus* L. The essential oils were reported to have 103 compounds composed of phenolic compounds and all oils belonged to the chemotype carvacrol and thymol. The *in vitro* phytotoxic action of three oils at 1000 ppm was reported to have antifungal properties affecting in seed germination and radicle growth of plants. Teixeira *et al*., (2013)[35] reported antioxidant potential and antibacterial action of essential oil from *Origanum vulgare*. The essential components are thymol, β-fenchyl alcohol, carvacrol γ-terpinene. The study suggested the hot water extract showed maximum anti-oxidant effects as compared to others. Anti-bacterial action was shown by all extracts causing maximum inhibition on Listeria strains. Falco *et al*., (2013)[36] investigated the chemical composition and biological activity of essential oils from flowers of *Origanum vulgare* L. under the different spatial distribution affecting its growth, soil covering, fresh biomass, essential oil amount and their composition were characterized by GC and GC-MS. The essential oils were identified as sabinenes and ocimenes. Martino *et al*., (2009)[37] suggested the role essential oils as natural preservatives for food products obtained from flowers of three *Origanum vulgare* L. ssp. hirtum (Link) Ietswaart samples. Three chemotypes were identified as carvacrol/thymol, thymol/α-terpineol and linalyl acetate/linalool respectively. These are also evaluated for anti-bacterial action. Then results contributed the remarkable relationship between chemical composition of essential oils and chemotypes in *Origanum vulgare* ssp. Hirtum. Mechergui *et al*., (2010)[38] screened the antioxidant potential of essential oils isolated from *Origanum vulgare* L. subsp. glandulosum (Desf.) Ietswaart collected from three localities of north Tunisia-Krib, Bargou and Nefza. The percentage yield was found out to be e p-cymene (36%, 40% and 46%), γ-terpinene (24%, 12% and 16%), thymol (32%, 39% and 18%) and carvacrol (2%, 2% and 15%) respectively. The isolated oils were characterized by GC and GC/MS, total phenolic content was also assayed by Folin–Ciocalteu method expressed in GAE varied from 9.37 to 17.70 g kg^{-1}. The antioxidant potential was performed by DPPH expressed in IC_{50} values ranging from 59 to 80 mgl^{-1}. Rodrigues *et al*., (2004)[39] performed sub- and supercritical CO_2 extraction of two different collected samples of Origanum at a temperature range of 293-313 k and 100 -200 bar pressure. The collected samples were commercial and cultivated under agronomic controlled. The different extracts of collected samples were analysed with the help of GC-MSD technique. The results showed greater yield in commercial sample as compared to cultivated. The chromatographic analysis showed essential oils identified as thymol with cis-sabinene in commercial and carvacrol with cis-sabinene hydrate in cultivated samples of Origanum. Milos *et al*., (2000)[40] isolated essential oils from leaves and flowers of *Origanum vulgare* L. and reported their anti-oxidant potential. Isolated essential oils comprising of glycosidically bound volatile oil and aglycones were identified as thymoquinone, eugenol, benzyl alcohol, 2-phenyl-ethanol, 3-hexen-1-ol, thymol and carvacrol. The antioxidant potential was performed by measuring peroxide values of lard stored at 60°C. Elshafie *et al*., (2017)[41] isolated essential oils as carvacrol, thymol, citral and limonene from aerial parts of *Origanum*

vulgare L. and reported their cytotoxic action on hepatocellular carcinoma cell Line HepG2. The results showed cytotoxic effect of plant due to presence of essential oils. Kubatka *et al*., (2017)[42] reported the chemopreventive potential of *Origanum vulgare* by NMU induced mammary tumour in rats. The results showed decrease in 55% tumour frequency and 44 % tumour volume as compared to control. Marrelli *et al*., (2016)[43] reported MTT assay on different plant species including *Origanum vulgare* analysed in MCF7, HepG2 (hepatic cancer) and LoVo (colorectal cancer) cell lines at 100 µg/mL. The results findings showed inhibition of cell proliferation by 47, 67, 39%, respectively. Koldas *et al*., (2015)[44] investigated anticancer activity of *Origanum vulgare* using different extraction solvents. The antiproliferative activity was performed by using xCELLigence real-time monitoring with different extracts (50 µg/mL to 250 µg/mL) of *O. vulgare*. Begnini *et al*., (2014)[45] isolated 4-terpineol (essential oil) using hydro-distillation method from aerials parts of *Origanum vulgare* and investigated its cytotoxic effects by using HT-29 (human colon adenocarcinoma) and MCF-7 cell line. It was found that 4-terpineol at concentration of 50 mg/ml significantly inhibited of growth of tumour cells by 60.8 and 48.9%, respectively. Berrington and Lall, (2012)[46] reported *in vitro* cytotoxicity in acetone extract of *Origanum vulgare* by using XTT assay in HeLa cells. The IC_{50} value is also performed and showed 126.3 ± 1.00 µg/mL. The results showed the extract increased the apoptosis

Table 1: Investigated the protective and cytotoxic action of selected herbs against HCC from Lamiaceae family and identified possible chemical compounds.

Scientific name	Common name/s	Part used	Identified possible chemical compounds	References
Ajuga bracteosa Wall. ex Benth	Buggleweed	Aerial parts	Neo-clerodane diterpenoids, phytoecdysteroids, steroids, sphingolipids, fatty acids, iridoids, triglycerides, phenylethanoid glycosides withanolides, quinols, ergosterol-5, 8-endoperoxide, phytoecdysones, borneol, hexadecanoic acid, camphor, β-eudesmol, trans-pinocarveol and α-guiaol.	[7-9]
Origanum vulgare Linn.	Oregano, Wild marjoram, Winter sweet	Aerial parts	Thymol, gama-terpinene, carvacrol, carvacrol methyl ether, cis-alpha bisabolene, eucalyptol, p-cymene, elemol, Chlorogenic acid, gentisic acid, rosmarinic acid and p-coumaric acid.	[10,11]
Roylea elegans Wall.	Ashy Roylea	Leaves	Pentacosane, octacosanol, friedelin, beta -amyrin, beta –sitosterol and betulonic acid.	[12]

Field view of *Ajuga bracteosa*

Figure 1: *Ajuga bracteosa* (Whole plant).

through morphological changes and reduced cytoplasmic membrane and cellular debris.

Roylea elegans Wall.

Roylea elegans commonly known as 'Patkarru' is erect 1-1.5 m high, bitter taste with lemon scented hoary shrub widely distributed throughout Himalayan region from Kashmir to Nepal at an altitude of 2,000-5,000 ft (Figure 3). Roylea is a genus of flowering plant belongs to mint family (Lamiaceae), first described as a genus in 1830.

It is a shrub of the monotypic genus and also known as *Roylea cineria* D. Don. It is a medium sized shrub reaching 1.7 m with finely tomentose branches.[47] Leaves are green to greyish color, 2.5-3.8 cm long with short stalk, hairy, ovate with apex acute or acuminate, crenate margin with base rounded. Flowers are five lobed, white tinged with pink with short axillary umbellate whorls. The calyx is cylindric, 10-nerved, erect and oblong. The petals are hairy with four stamens, unequal pairs, obtuse and smooth.[48] The plant contains essential oils, glycosides, diterpenes, flavonoids, tannins, steroids, saponins and phenolic compounds. The plant is well known for two furanoid diterpenes, royeleganin and royelegafuran.[49] Essential oils in plant comprises of betulin, beta-amyrin, beta-sitosterol, stigmasterol, cetyl alcohol, diterpenes such as calyenone, precalyone and calyone and triterpene as moronic acid.[50] The aerials parts are reported two new labdane diterpenoids named as cinereanoid A and cinereanoid B from the aerial parts of plant along with five known compounds such as β-sitosterol, stigmasterol, calyone, 1-methylindole-3-carboxaldehyde and pillion.[51] The leaves are used as bitter tonic and in febrifuge. The aerials parts are crushed and eaten with salt to strength the liver and their infusion are used in scabs and skin infections.[52] The tribal used whole crushed plant in liver disorders leaves is beaded into beads garlanded to infants against treatment of jaundice. The plant is used as traditional medicine in the prevention of diabetes, fever, jaundice, malaria, pimples, and flatulence. Leaves are also used as a blood purifier and in the treatment of cold and cough.[53]

Cytotoxic action of *Roylea elegans*

Bhatia *et al.*, (2020)[54] reported anti-proliferative and cytotoxic potential of the methanolic extract from leaves and stem of *R. elegans* by using L6 rat skeletal muscle cell line. The results showed the inhibited in the growth of L6 tumor cells with IC_{50} value of 69.41 µg/mL and 124.93 µg/mL and lactate dehydrogenase activity was reported as 20.29% and 0.3%, respectively.

DISCUSSION

HCC is an aggressive cancer that occurs in the setting of chronic liver disease and cirrhosis that frequently presents in advanced stages. Grandhi *et al.*, (2016)[55] stated that majorly up to 90% liver cancers detected as HCC across globally and only surgical resection and transplantation considered as mainstays for the

Field view of *Origanum vulgare* Linn.

Figure 2: *Origanum vulgare* Linn.

Figure 3: *Roylea elegans* (Whole plant).

treatment as option as primary approach. Secondary approaches such as palliative treatment and sorafenib therapy are acquired later after tumour development.

Hence, mechanism to reduce hepatoma aggressiveness via inhibition of cellular proliferation and treatment of HCC through modulation for oncogenic pathways stills remain a problem globally. The free radicals scavenging action of various phytoconstituents develops preventive role in various stages of HCC development such as initiation, promotion and progression. Moreover, the antioxidant potential of several phytoconstituents like flavonoids, poly-phenols, terpenes etc., are well known to possess hepatoprotective potential and prevention against Liver diseases. As a result, novel therapeutic strategies-especially those derived from organic plant compounds-are being investigated as possible supplements or substitutes for traditional medical care. Because of their potential as chemopreventive and therapeutic agents against HCC, members of the Lamiaceae family, which are abundant in bioactive Essential Oils (EOs) and phytoconstituents, have attracted a lot of attention.

Widely known for its aromatic species, the Lamiaceae family contains a wide variety of bioactive substances, such as terpenes, flavonoids, phenolic compounds, and essential oils, all of which have shown a number of anticancer effects. These include apoptotic, antioxidant, anticancer, and antiproliferative actions. The findings from the literature review highlight the significance of several Lamiaceae plants, including *Roylea elegans, Origanum vulgare* and *Ajuga bracteosa* in preventing the proliferation of cancer cells and offering hepatoprotective advantages.

Buggleweed, or *Ajuga bracteosa* reported a variety of biological properties, including as cytotoxic, antibacterial, and anti-inflammatory actions. The plant may be used as a chemopreventive drug since its essential oils, especially diterpenoids and sphingolipids, have been shown to have strong inhibitory effects on a number of cancer cell lines, including HepG2 (hepatocellular carcinoma). Further evidence for the possible therapeutic benefit of *Ajuga bracteosa* in the management of HCC comes from chemicals like β-sitosterol, which were extracted from this plant and have been shown to decrease tumour volume and frequency.

In a similar vein, oregano, or *Origanum vulgare*, which is well-known for its antimicrobial and antioxidant qualities, has shown remarkable cytotoxic effects on cancer cells. Research has shown that its essential oils, especially thymol and carvacrol, have antiproliferative properties through mechanisms such cell cycle arrest, apoptosis induction, and tumour cell metastasis suppression. The hypothesis that oregano, with its rich phytochemical makeup, could be a promising therapeutic agent against HCC is supported by the results from several *in vitro* investigations.

Additionally, *Roylea elegans* has demonstrated great promise as a possible anticancer herb. Diterpenes and flavonoids, two of its essential oils, have shown strong antiproliferative properties;

some of these components have been shown to stop the growth of different tumour cell lines. The plant's promise for managing HCC is further supported by its use in traditional medicine to treat liver conditions and jaundice. Even though preliminary research has demonstrated cytotoxicity, more investigation is required to identify the active ingredients and clarify their exact modes of action.

According to the results of the reviewed studies, these Lamiaceae plants exhibit anticancer properties through a number of intriguing methods. These include the capacity to regulate important cellular functions including apoptosis, cell cycle regulation, and angiogenesis, as well as antioxidant action, which is essential for preventing DNA damage brought on by oxidative stress. These herbs are very appealing for the prevention and treatment of HCC because of their capacity to increase the activity of liver detoxifying enzymes and guard against liver fibrosis. But even with the encouraging outcomes, there are still a number of unanswered questions regarding the full potential of Lamiaceae plants in the treatment of HCC. There is currently little data from clinical trials, and the majority of the evidence is based on *in vitro* and animal model studies. Furthermore, it is difficult to pinpoint the precise chemicals causing the noted anticancer effects due to the intricacy of the chemical makeup of essential oils and plant extracts. To ascertain these substances' effectiveness in people, more research is also required to understand their pharmacokinetics and bioavailability.

CONCLUSION

In conclusion, more thorough clinical research is required to confirm the efficiency and safety of the examined plants from the Lamiaceae family in human patients, even if they exhibit encouraging anticancer and hepatoprotective qualities. These plants are a great source of possible therapeutic agents for the prevention and treatment of hepatocellular carcinoma because of their widespread availability and diverse chemical makeup. Incorporating these plant-based substances into existing treatment plans may offer a more comprehensive and economical strategy for battling this debilitating illness.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

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