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Exploring the anticancer potential of *Boswellia serrata*: A comprehensive review

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Abstract

Plants are endowed with numerous phytochemicals and bioactive compounds which have been explored and reported to possess therapeutic potential against different diseases. The aim of this review paper is to explore the anticancer potential of *Boswellia serrata*. Cancer is known to be a burden on the global healthcare system while *Boswellia serrata* has been reported to possess numerous bioactive compounds with anticancer effects. Therefore, there is a need to further assess the applicability of *Boswellia serrata* as an anticancer. The included studies for review were accessed via online databases such as Scopus, PubMed, and Google scholar with specified inclusion and exclusion criteria to guide the study selection process. Following a critical content analysis, it was found that *Boswellia serrata* possesses numerous bioactive compounds with anti-proliferative, cell cycle inhibitory, apoptosis, anti-metastatic, and anti-tumor effect. In conclusion, *Boswellia serrata* holds a great potential in the treatment of cancer and can be a potent tool in the ongoing fight against cancer; however, further studies are essential to understand the mechanism of actions of specific bioactive compounds identified in *Boswellia serrata*.

Keywords: Anticancer; *Boswellia serrata*; Antimetastasis; Antitumor; Antiproliferative

1. Introduction

Globally, cancer has been a critical health issue and a burden to the healthcare system. In 2020, the World Health Organization reported about 10 million deaths globally due to cancer with the most common types being colon, breast, rectum, and prostate cancer [1]. This mortality rate has been forecasted to reach over 16 million by 2040 [2]. These data strengthen the claim that cancer has become a global health concern that requires proactive response from researchers, health professionals, governmental and non-governmental organizations, and other relevant stakeholders. Cancer can also be referred to as malignant tumors or neoplasm, which can affect any part of the body [3]. It is characterized by rapid and uncontrolled proliferation of abnormal cells, which have the capability to invade other body parts and spread to other vital body organs through a process known as metastasis.

The transformation of normal cells into tumor cells involve a comprehensive stage and interaction between individual genetic makeup and the external environment, which is constituted by carcinogenic agents [3, 4]. These carcinogenic agents can be of either physical, chemical, or biological [5]. Choi and Hua [6] identified the risk factors of cancer and reported that lifestyle has a crucial role to play in cancer cell formation. This lifestyle may include alcohol consumption, tobacco use, physical inactivity, unhealthy diet, and many more. In addition, Roderburg *et al.* [7] reported that in 2018, 13% of the globally diagnosed cancer cases were attributed to chronic infections caused by Human Papilloma Virus (HPV), hepatitis virus, *Helicobacter pylori*, and Epstein-Barr virus. Due to the complex nature of cancer, researchers have continuously worked towards the discovery of therapeutic agents with anti-cancer properties [8]. These efforts include the exploration of plants with medicinal properties. Similarly, the aim of this comprehensive review is to explore the

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anticancer potential of *Boswellia serrata*. The relevance of this is to contribute significantly to the ongoing effort to tackle the incidence and prevalence of cancer.

Boswellia serrata has been reported as a plant with various medicinal properties [9]. It is native to regions such as Africa, India, and the Arabian Peninsula, and widely used in Ayurveda, the traditional Indian medicinal system [9]. *Boswellia serrata* belongs to the family *Burseraceae* and genus *Boswellia*. It grows on dry mountainous regions of India, Northern Africa, and the Middle East [10]. The resinous part of the plant has been reported to contain monoterpenes (α-thujene), diterpenes (incensole oxide), triterpenes (α- and β-amyrins), pentacyclic triterpenic acids, and tetracyclic triterpenic acids [10]. Four pentacyclic triterpenic acids (Boswellic acids), extracted from the plants has been reported to possess anti-inflammatory and anticancer potential [11]. It has also been reported to be a potential anticancer agent [10]. In addition, the gum resin of *Boswellia serrata* has been shown to increase symptoms in patients with rheumatoid arthritis and osteoarthritis [12]. These are indications that *Boswellia serrata* possesses various medicinal properties and therefore, could be a potential therapeutic agent against cancer. This comprehensive review delves into the anticancer potential of *Boswellia serrata* by investigating its antiproliferative, cell cycle inhibitory, apoptosis, anti-metastatic, and anti-tumor potential. The finding of this report is relevant to the ongoing effort to drastically reduce cancer incidence, prevalence, and mortality rate.

2. Method

The methodology adopted by this study is a comprehensive review of scientific literature, which were accessed via online databases such as Scopus, PubMed, Google scholar, and Biomed central. Access to relevant resources via these databases provided insight into the medicinal use of *Boswellia serrata* within the context of cancer. Furthermore, relevant websites such as www.theplantlist.org and www.ipni.org provided vital information about the dynamics and potential of *Boswellia serrata*. The various resources included for critical review are published articles, thesis, abstract, published books, and conference proceedings.

The inclusion criteria, which served as a guide for the study selection process, include studies published between 2010 to 2024, studies published in English language, and studies that focus on either cancer, *Boswellia serrata*, or both. On the other hand, studies published earlier than 2010, in language other than English, and without a focus on the anticancer potential of *Boswellia serrata* were excluded. A critical aspect of the study selection process was the prioritization of only quality studies that have satisfied the inclusion criteria. Search terms include "*Boswellia serrata*," "anticancer properties," "*Boswellia serrata* and cancer," "anti-proliferation," "cell cycle inhibition," "apoptosis inducer," "anti-metastatic potential," and "anti-tumor effect". The major findings extracted from the included studies are then systematically presented in this report.

3. Discussions

This section discusses the major findings from a critical review and analysis of the included studies. These findings are presented in the subsections below:

3.1. Overview of *Boswellia serrata*

Boswellia serrata, commonly known as Indian Frankincense is an indigenous traditional plant to India, Asia and Northern Africa. It is known for its medicinal, commercial and religious uses, hence making it a highly valued plant. It belongs to the family of *Burseraceae* and has been used for centuries in traditional Ayurvedic medicine in the treatment of a variety of diseases such as Osteoarthritis, Inflammatory bowel disease, Asthma, and Rheumatoid arthritis [13]. Trade routes stretching from Dhofar (Oman), Qarn (Yemen), to Saukin (Ethiopia) facilitated the exchange of Boswellia resin with empires like Persian, Greek, Babylonian, Chinese, and Mesopotamian. *Boswellia serrata* resin, among others, held substantial value in these ancient trade networks, contributing to cultural and economic interactions among varied civilizations [14,15].

Boswellia trees, known for their deciduous nature, can grow to heights exceeding 5 meters, influenced significantly by their species and the surrounding conditions. These trees present smooth stems and branches, with bark that sheds, giving them the appearance of either a bush or a tree [16]. It often reaches a height of 9 to 15 metres and a diameter of 1.2 to 1.8 metres. The thin bark has ashy, reddish, or greyish-green tones, and under its outer layer lies a layer of chlorophyll that peels off in tiny, papery flakes. Their fruits are typically 1.3 centimeters long, trigonous, and has three valves, three heart-shaped, one-seeded pyrenes, and wings along the edges. *B. serrata* has alternating, stipule-free, imparipinnate leaves that range in length from 20 to 45 centimeters. These leaves tend to cluster towards the tips of branches, with leaflets spanning 17-31 cm. The leaflets are positioned opposite each other, varying in size from 2.5-8

cm in width and 0.8-1.5 cm in breadth, with the lower pairs often being the smallest. They exhibit significant variety in their size and are sessile, lanceolate, ovate-lanceolate, and have an uneven, notched border [17]. Both the exudate from its bark (resin of the oleo gum) and leaf extracts have shown various biological activities such as anti-inflammatory, anti-oxidant and anti-cancer [18,19,20]. Table 1 presents the taxonomical hierarchy while Table 2 presents the geographical nomenclature of *Boswellia serrata*

Table 1 Taxonomical Hierarchy of *Boswellia serrata*

Kingdom	***Plantae***
Phylum	*Tracheobionta*
Class	*Magnoliophyta*
Order	*Magnoliopsida*
Family	*Sapindales*
Genus	*Burseraceae*
Species	*Boswellia serrata*

(Source: [21])

Table 2 The geographical nomenclatures of *Boswellia serrata* tree

English	**Indian Olibanum, Indian Frankincense**
India/Hindi	Salai
Bengali	Kundur, salai
Arabic	Kondor, luban dhakar
Telugu	Andugum chettu

(Source: [21])

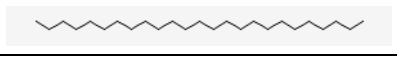
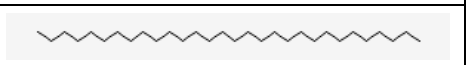
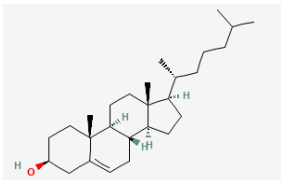
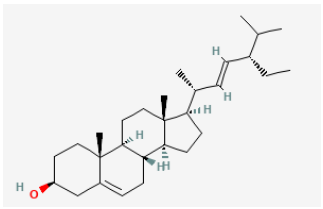
Figure 1 *Boswellia serrata* tree in its Natural Habitat (Source: Forrest Ecology)

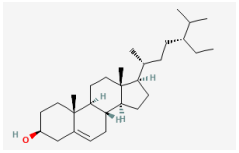
3.2. Bioactive Compounds of *Boswellia serrata*

The Oleo gum resin of *Boswellia serrata* has been analyzed by various studies in an attempt to understand the various bioactive compounds that constitute the medicinal plant. According to Sudhanshu *et al*. [22] the plant possesses several pharmacologically active elements such as terpenoids and oil. However, several factors affect the chemical composition of the plant and these include species, age, resin quality, and geographic location [23]. Specifically, the oleo gum contains resins (30–60%), essential oil (5–10%), and water-soluble polysaccharides (~65% arabinose, galactose, and xylose) [22]. Hanaa *et al*. [24] conducted a GC/MS analysis of unsaponifiable matter of petroleum ether extract of *B. serrata* oleum gum resin and the bioactive compounds discovered are presented in Table 3. The study also analyzed fatty acid methyl esters of petroleum ether extract of the plant with the identified bioactive compounds presented in Table 4. Lastly, the compounds identified through a GC/MS analysis of the volatile oils of *B. serrata* Oleo gum resin and 11 bioactive compounds were identified (Table 5).

Boswellia serrata is known for containing resinous compounds, and the identified hydrocarbons are likely components of the resin. These hydrocarbons contribute to the overall chemical profile of the gum resin. Sterols are common components in plant resins and oleo-gum resins. Cholesterol, stigmasterol, and β-sitosterol are plant sterols that may have physiological roles in the plant and can be transferred to the oleo-gum resin [10]. The significant presence of tricosane (75.32%) suggests that it is a major constituent of the unsaponifiable matter in *Boswellia serrata* [24]. Tricosane may contribute to the resin's properties and play a role in its biological functions. The justification for the presence of these compounds lies in the plant's biosynthetic pathways and ecological functions. Hydrocarbons are often synthesized as part of resinous compounds that protect plants from herbivores and pathogens [25]. Sterols, on the other hand, are essential components of cell membranes and play various roles in plant physiology [26]. This is presented in Table 3 below

Table 3 GC/MS analysis of unsaponifiable matter of petroleum ether extract of *B. serrata* oleum gum resin

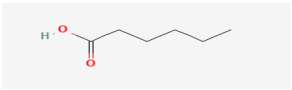
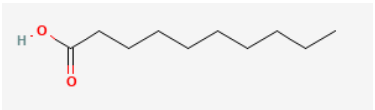
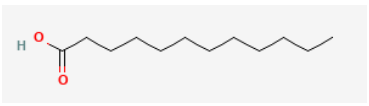
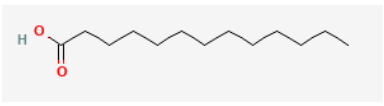
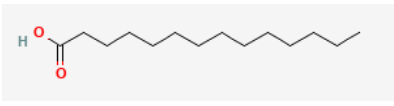
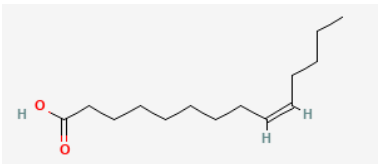
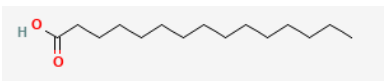
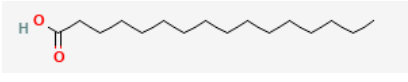
Retention Time	Compound	Composition (%)	Structure
17.22	Eicosane	3.19	
17.92	Heneicosane	4.61	
20.91	Tricosane	75.32	
21.75	Tetracosane	8.47	
22.51	Pentacosane	2.67	
23.34	Hexacosane	2.58	
24.61	Octacosane	1.16	
27.91	Triacontane	1.11	
28.72	Cholesterol	0.14	
30.07	Stigmasterol	0.58	

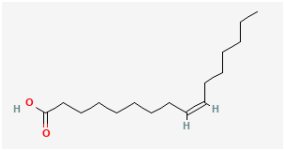
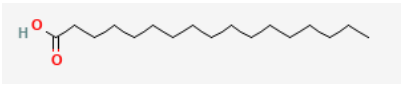
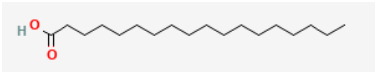
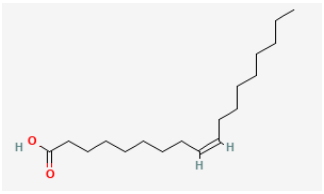
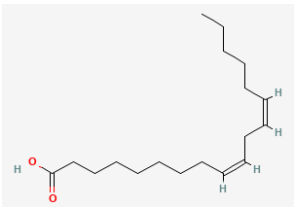
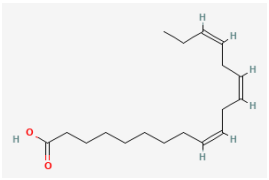
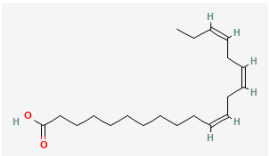
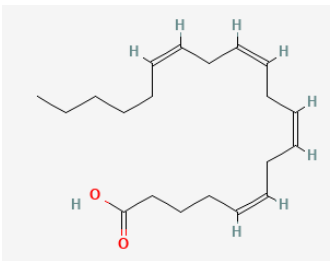
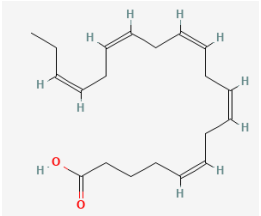
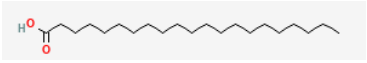
30.73	β-Sitosterol	0.17	

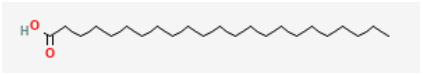
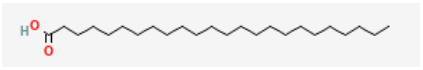
(Sources: 24; 10)

The GC/MS analysis of the fatty acids methyl esters (FAMEs) in the petroleum ether extract of *Boswellia serrata* oleo-gum resin reveals a diverse and intricate chemical composition. The identified compounds include both saturated and unsaturated fatty acids, with Lauric acid (C12:0), Myristoleic acid (C14:1), Palmitoleic acid (C16:1), Oleic acid (C18:1), and Linoleic acid (C18:2) being among the major constituents [24]. These fatty acids are known for their various biological activities, including antimicrobial, anti-inflammatory, and cardiovascular benefits [27]. The presence of Lauric acid suggests a potential role in the plant's defense against microbial threats, while Myristoleic acid and Palmitoleic acid may contribute to anti-inflammatory and skin health properties [28]. Oleic acid, a common monounsaturated fatty acid, is abundant and likely contributes to the overall health-promoting characteristics of the resin. Additionally, the presence of essential fatty acids like Linoleic acid and Linolenic acid underscores the nutritional value of *Boswellia serrata* oleo-gum resin. The resin also contains long-chain polyunsaturated fatty acids, such as Arachidonic acid and Eicosapentaenoic acid, which are precursors to bioactive lipid mediators involved in inflammation and immune response [29]. This is presented in Table 4 below

Table 4 GC/MS Analysis of Fatty Acids Methyl Esters of Petroleum ether Extract of *B. serrata* Oleo Gum Resin

Retention Time	**Compound**	**Composition (%)**	**Structure**
6.05	Caproic acid (C6:0)	0.08	
15.06	Capric acid (C10:0)	0.51	
18.27	Lauric acid (C12:0)	9.38	
19.63	Tridecanoic acid (C13:0)	0.68	
21.32	Myristic acid (C14:0)	0.32	
22.03	Myristoleic acid (C14:1)	9.3	
24.3	Pentadecanoic acid (C15:0)	0.51	
28.17	Palmitic acid (C16:0)	2.24	

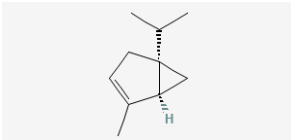
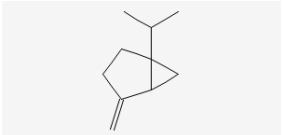
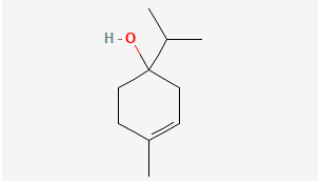
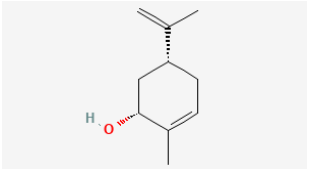
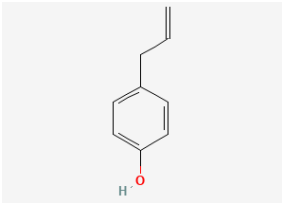
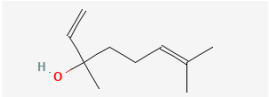
29.38	Palmitoleic acid (C16:1)	22.41	
31.62	Margaric acid (C17:0)	4.54	
33.1	Stearic acid (C18:0)	3.02	
34.79	Oleic acid (C18:1)	30.05	
35.41	Linoleic acid (C18:2)	3.39	
35.92	Linolenic acid (C18:3)	1.61	
40.8	Arachidic acid (C20:0)	1.6	
41.23	11,14,17-Eicosatrienoic acid (C20:3)	2.38	
42.05	Arachidonic acid (C20:4)	3.2	
44.56	5,8,11,14,17-Eicosapentaenoic acid (C20:5)	1.91	
45.17	Heneicosanoic acid (C21:0)	1.8	

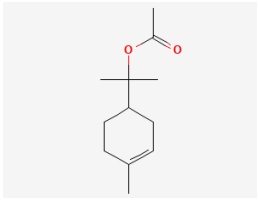
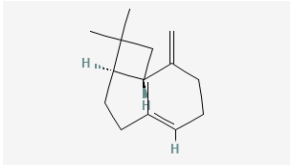
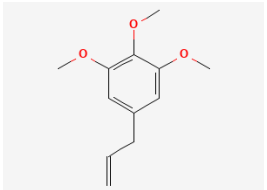
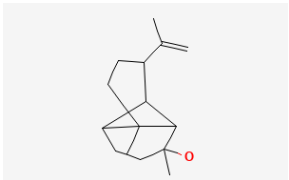
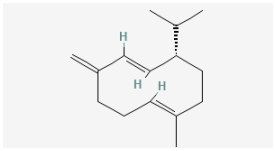
48.55	Tricosanoic acid (C23:0)	0.68	
50.36	Tetracosanoic acid (C24:0)	0.27	

(Sources: 24; 10)

The GC/MS analysis of the volatile oils in *Boswellia serrata* oleo-gum resin reveals a diverse array of compounds, each contributing to the resin's unique aromatic profile. Sabinene dominates the composition at 19.11%, suggesting a prominent role in defining the resin's fragrance [24]. Terpinen-4-ol and β-Copaen-4-α-ol follow closely, with percentages ranging from 10.24% to 14.64%, contributing to the overall complexity of the volatile oil blend [10]. Terpinyl acetate, a terpene ester at 13.01%, enhances the aromatic richness of the resin. Additional compounds such as Elemicin, Germacrene D, and β-Caryophyllene contribute to the resin's volatile oil composition, each adding distinct olfactory and potentially therapeutic characteristics [23]. The presence of these volatile oils suggests potential applications in traditional medicine and perfumery, aligning with the resin's historical uses. The resin's aromatic complexity, derived from compounds like Chavicol, Linalool, and α– Thujene, further underscores its potential versatility in various applications. This is presented in Table 5 below

Table 5 GC/MS Analysis of the Volatile Oils of *B. serrata* Oleo gum Resin

Retention Time	Compound	Composition (%)	Structure
6.74	α– Thujene	1.29	
9.13	Sabinene	19.11	
13.52	Terpinen-4-ol	14.64	
16.2	cis-Carveol	6.26	
16.9	Chavicol	4.75	
18	Linalool	1.02	

22.37	Terpinyl acetate	13.01	
24.1	β-Caryophyllene	3.03	
31.2	Elemicin	7.05	
31.43	β-Copaen-4-α-ol	10.24	
37.13	Germacrene D	12.6	

(Sources: 24; 10)

3.3. Anticancer Potential

The focus on plant-based treatments in cancer research is promising due to the presence of chemical constituents within plants showing a more targeted effect on cancer cells while potentially minimizing harm to healthy cells. This targeted action is one of the key aspects that make plant-based therapies an exciting area of exploration in cancer treatment. *Boswellia serrata* demonstrates a multifaceted anti-cancer mechanism, encompassing cell cycle inhibition, apoptosis induction, anti-proliferative effects, and exerting anti-tumor actions. [29, 30].

3.3.1. Anti-Proliferative Effects

The antiproliferative effects of *Boswellia serrata*, particularly its boswellic acids, have been explored in clinical trials and in-vitro studies. The process by which a cell grows and divides to produce two daughter cells is known as cell proliferation. It encompasses the fusion of the cell cycle and growth, resulting in a large number of diploid cell progenies. The external growth factors and the intracellular gene regulatory network closely regulate this process. Cancer cells are recognized for their capability to evade growth suppressors, leading to traits such as replicative immortality and continuous cell proliferation [31, 32].

Current research findings in clinical trials for patients with breast cancer suggest that the boswellic acids derived from *Boswellia serrata* exhibit potential antiproliferative effects. According to Valente *et al*. [31], an early-phase clinical trial was conducted to investigate the biological activity and safety of *Boswellia serrata* (*B. serrata*) in patients with invasive breast cancer, prior surgery, patients were administered an oral dose of 2400 mg/day. The examination of diagnostic and post-treatment tissues revealed a significant decrease (13.8%) in proliferation (Ki-67 index), contrasting with the control group which showed an increase in proliferation (54.6%). The administration of *B. serrata* was reported to be well-tolerated, with no adverse events recorded [31].

In an in-vitro study by Shao *et al.* [32] on the Inhibitory Activity of Boswellic Acids from *Boswellia serrata* against Human Leukemia HL-60 Cells in Culture, four Boswellic acids compounds (β-3-Boswellic acid, 3-O-Acetyl-β-3-boswellic acid,

11-Keto-β-3-boswellic acid, and 3-O-Acetyl-1l-keto-β-3-boswellic acid) were isolated from *Boswellia serrata* oleogum resin. Their inhibitory activity was demonstrated in Human Leukemia HL-60 Cells and a dose-dependent inhibition of DNA, RNA, and protein synthesis in HL-60 cells was reported [32]. These findings suggest the potential of *Boswellia serrata* in exerting antiproliferative effects, making it a subject of interest for further research and development in cancer therapy.

3.3.2. Cell Cycle Inhibitory Activities

Cell cycle inhibition, which can happen at different phases of the cell cycle, is crucial for preserving healthy cell function and halting the uncontrolled proliferation of cells. DNA synthesis and chromosome segregation are carefully monitored at cell cycle checkpoints to detect abnormalities (mutation). If mutation is detected in a normal cell undergoing the cell cycle, the cell cycle will arrest to allow for the repair of the mutation before re-entering the cell cycle. In contrast, cancer cells can harbor mutations in their DNA yet undergo cell cycle without arrest [33, 34].

The findings of a previous study conducted by Lv *et al*. [35] have indicated that Acetyl-11-keto-β-boswellic acid (AKBA) can enhance the sensitivity of cisplatin (CDDP) by inducing G0/G1 phase arrest in A549 cells. To assess the impact of AKBA, CDDP alone, and their combination on the cell cycle in A549 cells, flow cytometry was employed. After a 48-hour cotreatment with AKBA and CDDP, flow cytometry analysis revealed an increase in the percentages of cells in the G0/G1 phase and a reduction in the frequencies of cells in the G2/M phase compared to CDDP alone. This suggests that the combined treatment inhibits the transition of cells from the G0/G1 phase to the G2/M phase in the cell cycle [35].

It was also reported in another investigation by Lv *et al*. [35] that AKBA Induced the Cell Cycle Arrest at G0/G1 Phase in Human NSCLC Cell Line A549. Flow cytometry analysis was conducted to assess the cell cycle distribution in A549 cells treated with different concentrations of AKBA (0, 5, 10 μg/mL). Their result indicated that AKBA led to an increase in the percentage of cells in the G0/G1 phase and a decrease in the S phase at the concentration of 10 μg/mL. The percentage of cells in the G2/M phase, however, barely changed. The Western blotting technique was also utilized to examine the levels of cell cycle proteins/cell cycle regulators, and it was reported that AKBA downregulated the expression levels of cyclin A2 and cyclin E1. The investigation of the expression of the cell cycle protein further aligned with the results obtained from flow cytometry, providing additional evidence of AKBA's inhibitory effect [36]. These findings strongly suggest that AKBA can inhibit tumor cell growth by inducing cell cycle arrest specifically at the G0/G1 phase.

3.3.3. Apoptosis Inducer

Apoptosis, a tightly regulated mechanism of programmed cell death, is crucial for maintaining tissue homeostasis and eliminating damaged or unnecessary cells [37], such as those resulting from DNA damage or during development [38, 39]. Many Phyto-compounds have been investigated for their potential to induce apoptosis, among them is Acetyl-11-keto-β-boswellic acid (AKBA), a pentacyclic terpenoid derived from the resin of the Ayurvedic medicinal plant *Boswellia serrata* [40]. AKBA, known for its anti-inflammatory properties, demonstrates significant cytotoxic effects on various human cancer cell lines, including glioblastoma, meningioma, leukemia, breast, liver, fibrosarcoma, melanoma, colon, prostate, and pancreatic cancer cells [41- 45], through the activation of caspase-3 and caspase-8 as well as with poly (ADP) ribose polymerase (PARP) cleavage [46, 47] and the modulation of the death receptor 5-mediated signaling pathway [47].

Previous studies have shown a significant increase in apoptosis within colorectal [43 - 48] breast [49] oral squamous cell [50] carcinomas, upon administration of oleoresin from Boswellia species extract, particularly *Boswellia serrata*. However, the precise pathways and molecular mechanisms underlying the process remain unclear [51]. In 2002, Liu *et al*. conducted a study (as cited in [47]) examining the apoptotic and antiproliferative impacts of three principal components of *Boswellia serrata* extract - β-boswellic acid (BA), keto-β-boswellic acid (K-BA), and acetyl-keto-β-boswellic acid (AK-BA) - on colon cancer HT-29 cells, which are a line of human colorectal adenocarcinoma cells. The results revealed that both K-BA and AK-BA dose- dependently increased the cytoplasmic DNA–histone complex in HT-29 cells, with AK-BA exhibiting a stronger effect than K-BA. BA only showed an apoptotic effect at the highest concentration tested. Flow cytometry analysis showed that after incubation with 100 μM K-BA and AK-BA for 24 hours, the number of apoptotic cells significantly increased, with AK-BA inducing a larger proportion of sub-G1 cells compared to K-BA. However, BA did not show a significant increase in the sub-G1 peak at the same concentration. To further confirm the apoptotic effects of BA in HT-29 cells, Liu and his colleagues evaluated the activation of caspase-3 induced by AK-BA compared to camptothecin. The results indicated that at 50 μM, both effects of AK-BA were more than 3-fold greater than those induced by camptothecin. In the same year, Liu and his team also investigated the impact of BA, K-BA, and AK-BA on Hep G2 cells (as cited by [47], [52]). The findings indicated that a 100 μM concentration of AK-BA

significantly elevated the sub-G1 peak, whereas K-BA did not exhibit a notable apoptotic effect at the same concentration.

Conti *et al*. [41] also observed that the treatment of 30 μM AKBA to A172 cells resulted in a 12% increase in apoptotic cells compared to the 3% observed in untreated cells. Similarly, Li *et al*. [53] conducted a study examining the mechanism of AKBA-induced apoptosis, measuring caspase-3/7 activity and analyzing the cleavage of caspase 3 and PARP. Their findings demonstrated an elevation in the percentages of early apoptotic, late apoptotic, and necrotic cells in U251 and U87-MG cells following AKBA treatment.

3.3.4. Anti-Tumor Effects

Boswellic acid and its structurally related derivatives have been documented to be effective as an anti-inflammatory, hypolipidemic, and immunomodulatory [54]. Various triterpenoid acids identified in both *B. serrata* and *B. carterii* have been recognized for their anti-proliferative properties [55], and in vivo studies have also confirmed that AKBA possesses anti-carcinogenic and anti-tumor properties [20, 21, 53]. A study conducted by Li *et al*. [53] showed a significant inhibition by AKBA in the migration and invasion of U251 and U87-MG cells and also reduced colony formation observed in cells treated with 10, 20, and 30 μM AKBA compared to the control group, suggesting that AKBA has the potential to significantly block the metastatic biological functions of glioblastoma cells. Acetyl-11-keto-beta-boswellic acid (AKBA) exhibited greater efficacy in inhibiting cancer cell growth compared to the isolated pure form of 3-O- acetyl-11-keto-beta-boswellic acid, as reported by Al-Yasiry and Kiczorowska [55].

Conti *et al*. [41] investigated the combined impact of AKBA and ionizing radiation on the viability of glioblastoma cells, including U87, U251, LN319, and A172. The study involved irradiating the cells with varying doses (2, 4, or 6 Gy) followed by exposure to different AKBA concentrations (10–50 μM) for 72 hours. AKBA treatment demonstrated a dose-dependent inhibition of survival across all tested cell lines (10–50 μM). A172 and LN319 cells exhibited higher susceptibility to the treatment compared to U87 and U251 cells. Notably, AKBA significantly reduced the survival of A172 cells by over 50% at a concentration of 30 μM, while the inhibitory effect in the other three cell lines was achieved at the higher AKBA concentration of 40 μM. The study suggested that the combination of radiation and *Boswellia serrata* extract (AKBA) could be a potential cancer treatment, exhibiting a more substantial inhibitory effect compared to radiation alone. Existing evidence supports the anti-cancer potential of boswellic acid against various malignant tumors, with numerous semi-synthetic boswellic acids showing notable cytotoxic effects [11, 56-58].

3.3.5. Anti-Metastasis Potential

Metastasis, a hallmark of cancer progression, involves the spread of cancer cells from the primary tumor to distant sites, contributing significantly to the malignancy of the disease [59]. Targeting metastasis is recognized as promising for advancing cancer treatment, as emphasized by Esposito *et al*. [60], and numerous medicinal plants have been investigated for their potential capabilities in inhibiting metastasis in various tumor cancers (breast, hepatic, colon, and stomach cancer) [61, 62]. A study conducted by Yadav *et al*. [63] revealed that the oral intake of AKBA at doses ranging from 50 to 200 mg/kg exhibited a dose-dependent suppression of colorectal cancer (CRC) tumor growth in mice. This led to a reduction in tumor volumes (8.91 ± 0.41 mm^3 to 4.16 ± 0.19 mm^3) compared to mice treated with the vehicle. It was also observed that AKBA exhibited high efficacy in suppressing ascites and distant metastasis to the liver, lungs, and spleen in orthotopically implanted tumors in nude mice when compared to the control group.

Several studies have suggested that cancer cells possess chemokine receptors responsible for facilitating metastasis to specific organs where their corresponding chemokines are expressed [64]. Chemokines and their receptors have been identified to play a key role in the initiation or progression of cancers of the lung, colon, liver, breast, cervix, prostate, bladder, ovary, esophagus, skin, and lymphatics cancer [65]. Early work has shown elevated expression levels of chemokine receptors, namely CXCR4, CCR7, CCR9, and CCR10, in cancer cells originating from various solid tumor types [66]. Among the most studied chemokines involved in tumor cell migration and metastasis is stromal cell-derived factor 1α (SDF-1 α, also recognized as CXC chemokine ligand 12 [CXCL12]) and its corresponding receptor, CXCR4. In a study led by Park [67], the investigation focused on whether AKBA could influence the expression of CXCR4, thereby hindering tumor cell invasion. The findings show that AKBA effectively downregulates constitutive CXCR4 expression in various tumor cells characterized by an overexpression of this chemokine receptor, which led to the inhibition of CXCL12-induced invasion in pancreatic (AsPC-1, BxPC-3, MIA PaCa-2, and PANC-28) and breast (MDA-MB-231, MCF7/Neo, MCF7/HER2, SKBR3) cancer cells. Also, when treated with 50 μmol/L AKBA for 12 hours, AKBA demonstrated the ability to downregulate CXCR4 expression in leukemia (KBM-5), kidney (A293), and multiple myeloma (U266) cancer cell lines. However, it is noteworthy that the extent of CXCR4 downregulation by AKBA is not uniform but depends on the specific cell type.

4. Conclusion

This report has provided a comprehensive insight into the therapeutic potential of *Boswellia serrata* as an anticancer agent. Through a systematic review of relevant studies, this report has further strengthened the claim that *Boswellia serrata* possesses numerous bioactive compounds with anti-proliferative, cell cycle inhibitory, apoptosis, anti-metastatic, and anti-tumor effect. However, further studies are essential to understand the mechanism of actions of specific bioactive compounds identified in *Boswellia serrata*.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

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