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A REVIEW ARTICLE ON THE POTENTIAL ROLE OF BOSWELLIC ACID IN PREVENTION AND TREATMENT OF CHRONIC AND INFLAMMATORY DISEASES

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ABSTRACT

Boswellic acids are pentacyclic triterpenes, Belongs to the active pharmacological compounds of oleo gum resin of different Boswellia species of the family Bursuraceae. Among the various boswellic acids,11-keto-beta-Boswellic acid (KBA) and acetyl-11-keto-beta-boswellic acid(AKBA) are pharmacologically active and potent inhibitors of 5-lipoxygenase.Animal experiments show the anti-inflammatory activity of the extract. The action is due to several mechanisms of boswellic acid, such as the inhibition of lipoxygenase and reduce the synthesis of prostaglandin. The pharmacological activity of boswellic acid was also evaluated by both preclinical and clinical studies. Boswellic acd is attributed to its ability to induce anti-inflammatory, expectorant, anxiolytic, analgesic, tranquilizing and anti-bacterial effects.

KEY WORDS: Boswellic acid, acetyl-11-keto-beta-boswellic acid,11-keto-beta boswellic acid, chronic diseases, lipoxygenase, molecular targets, inflammation.

INTRODUCTION

Chronic disease can be defined as a physical or physiological state that leads to functional limitations or requires a constant observation or treatment for long time period. Globally, chronic diseases have hindered health and living conditions of many. Many of the universally used clinical drugs (especially biological ones) these days have deficiencies of side effects and the high cost of treatments. Therefore numerous natural compounds, which have been identified as potent signalling modulators and The epigenetic pathways that lead to cancer are currently under development.

Natural products have gained considerable attention as they are abundant. Sources of various compounds which can function as biologically active drugs against different chronic diseases. This plant derived molecules have significantly improved the existing medicinal system. For example, in a developing nation like India, about 65% of the country's population benefits from the use of phytomedicines that play an essential role in the health management system, satisfactory. In developed nations like the United States, the sale of phytomedicine has registered steep slope in recent years. The study shows that around 80% of population of Africa use phytomedicines to meet their health care needs. According to WHO, almost 80 of the world's population uses phytomedicines for their management of various ailments.

Boswellic acid is one of those phytochemicals, obtained from the rubber resin of Boswellia species that possibly help in treatment of different chronic diseases, Cosmetic preparations, coating materials, incense used in cultural rites and rituals and many more. It is one of the most essential and commonly used components in conventional Ayurvedic and unani drugs. It have been shown be extremely effective in relieving numerous inflammatory, gastrointestinal, hormonal and microbial diseases. It is said that the conventional drugs has the properties of an anti-inflammatory, antiseptic, ,24-dihyrexpectorant, anxiolytic, antineurotic, analgesic and tranquilizer. The studies established that it exhibits substantial potential in the management of inflammation and several medical conditions.

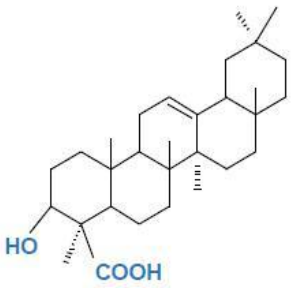
SOURCE AND COMPOSITION

BA comprises a series of pentacyclic triterpene molecules, generated by the trees in the genus Boswellia, usually known as Indian oliabanum, salai guggal, loban or kundur, and is found to be effective against many diseases. Categorized under Burseraceae family, these are moderate to large-sized branching trees prevailing over the mountainous regions of India, North Africa, and the Middle East. (figure 1) The genus Boswellia consist

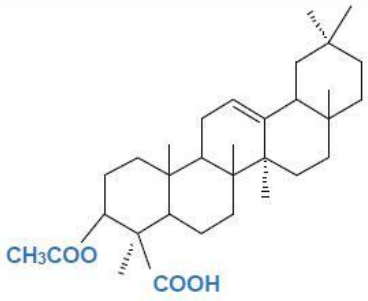
of roughly 25 species widely dispersed in Arabia, the North-eastern coast of Africa and India.[1]

(Figure 1)

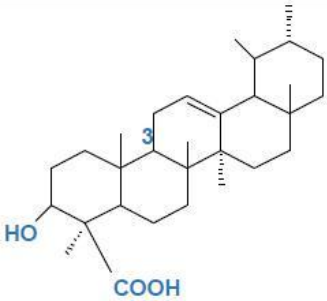
Boswellic acids with the molecular formula $C_{32}H_{52}O_4$ of the main asset incense components. The four main Boswellic acids found in the incense are: β-Boswellic acid (BA), acetyl-β-Boswellic acid (ABA), 11-keto-β-Boswellic acid (AKBA), which has been shown to be responsible for the inhibition of proinflammatory enzymes.[2] Several added BAs extracted from the Boswellia are 9,11 -dehydro-α-BA and 9,11-dehydro-β-BA and their respective acetylated forms acetyl-9,11 -dehydro-α-BA and acetyl-9,11-dehydro-β-BA. Some additional chemical components of Boswellia include lupeolic acid nad acetyl-lupeolic acid, incensole acetate, incensole oxide and isoincensole oxide. Studies also described the incidence of a pentacyclic triterpenodiol combination of 3α,24-dihydroxyrus-12-eno and 3α,24-dihydroxyolean-12-eno, serratol, α-thujene, tirucall-8,24-dien-21-oic, d-G oils, α-pinene and octyl acetate in the crude Boswellia rubber resin extract. (figure 2) However, KBA and AKBA has proven to be the most powerful in the negative regulation of the production of cytokines and inhibiting the enzymes responsible for inflammatory responses. Therefore, these have been reported as efficient therapeutics against different chronic diseases.[2]



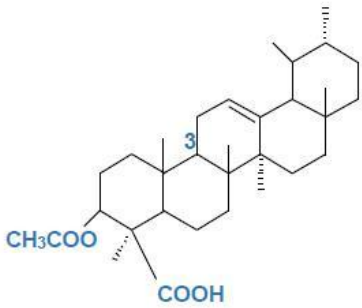
α- Boswellic Acid



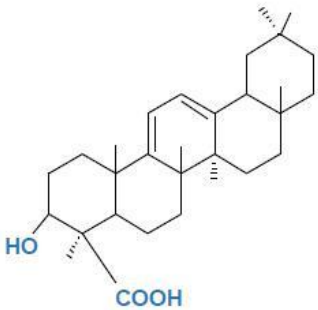
Acetyl-α- Boswellic Acid



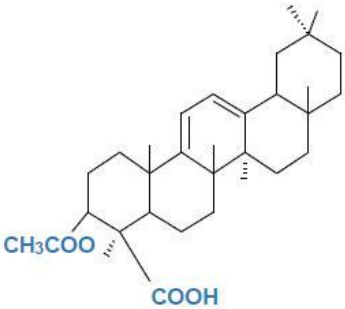
β- Boswellic Acid



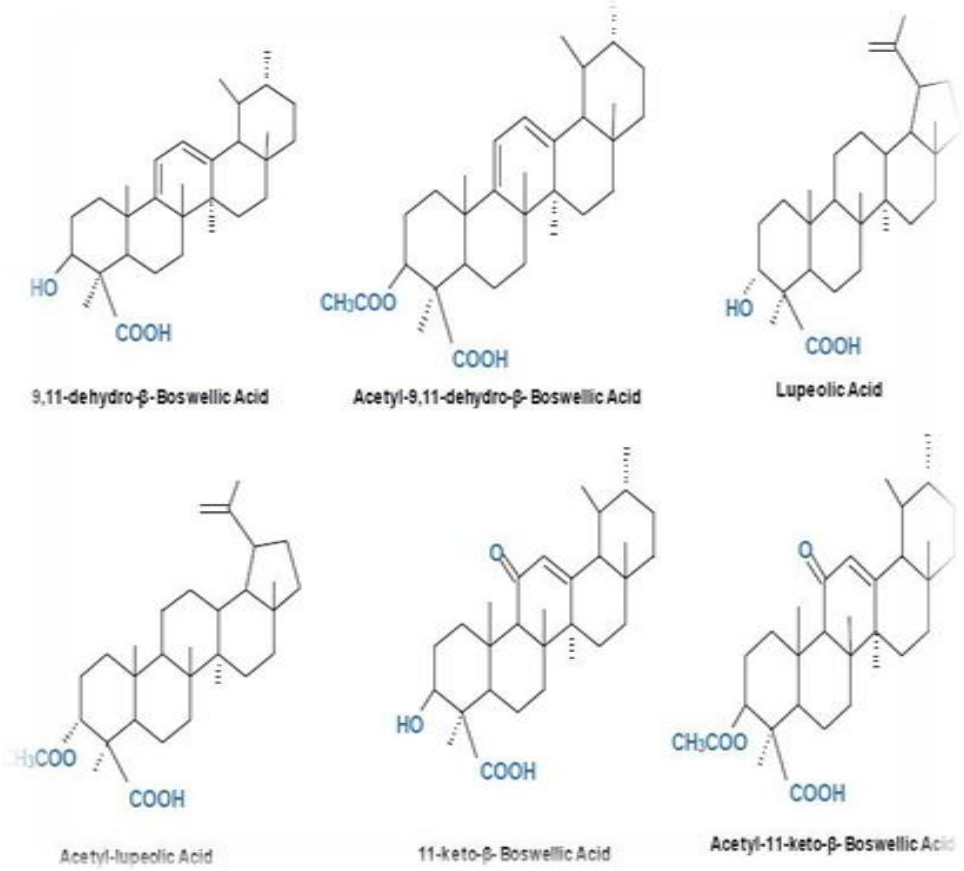
Acetyl-β- Boswellic Acid



9,11-dehybro-α- Boswellic Acid



Acetyl-9,11-dehydro-α- Boswellic Acid



(Figure 2)

PHARMACOLOGICAL ACTIVITY OF BOSWELLIC ACID

The pharmacological activities of BA are attributed to its aptness to induce anti- inflammatory, expectorant, antiseptic, anxiolytic, anti-neurotic, analgesic, tranquilizing, and antibacterial effects.[3] It can modulate diverse targets such as enzymes, growth factors, kinases, and transcription factors, as well as receptors, which allow it to stimulate apoptosis, cell cycle arrest, etc. It can also inhibit different signalling pathways[1] related to cell survival[4], proliferation[5], and metastasis.[6]

POTENTIAL ROLE OF BOSWELLIC ACID IN THE TREATMENT OF CHRONIC DISEASES

As mentioned earlier, BA is a multi-purpose compound, which allow its use against various diseases. The BA's perspective in the management of various chronic diseases are well evidenced by a series of preclinical studies through their ability to modulate multiple mediators involved in the pathogenesis of various diseases.

Arthritis

Arthritis arises mainly due to inflammation of joints and the connective tissues surrounding them. Osteoarthritis, being the predominant of all forms, affects a wide range of the population worldwide.[7] A study on the effect of BAs in bovine serum albumin (BSA)-induced arthritis reported that on oral administration, BAs (25, 50, and 100 mg/kg/day) significantly mitigated the leucocyte population and inhibited its infiltration into the knee joint as well as the pleural cavity in a BSA-injected knee. In addition, the electrophoretic pattern of the proteins present in the synovial fluid was altered.[8] Also, when BA was conjugated with an active metabolite Rhein and administered at the specified dose level of 15.73 mg/kg, p.o. (BID), it reduced the diameter of the knee and normalized the biochemical and haematological abnormalities in rat models of collagenase-induced osteoarthritis. Another study showed that under topical treatment, the concentrations of BA in synovial fluid increased from two- to six-times as compared to their plasma level. It was found that cartilage loss in mice was reduces considerably after oral or topical treatment with BAs compared to vehicle control.[9]

Asthma

Asthma is increasing as a serious global health problem, which is characterized by airway hyperreactivity, airway inflammation, improved mucus production, airway epithelial wall detachment, and an increase in the IgE levels. An investigation on the anti-asthmatic potential of BA in a murine model of asthma reported suppression of allergic airway inflammation, AHR, OVA-specific IgE,

and Th2 cytokines secretion were in treated groups. In addition, the expression of p- STAT6 and GATA3 were also suppressed in a dose-dependent manner.[10] In another in vivo study, the effect of BA was analysed by injecting a sensitization liquid (0.15 mL aluminium hydroxide gel at 88.67 mg/mL and 0.05 mg ovalbumin) intraperitoneally in an asthma model, and it was found to minimize the symptoms by abrogating p-STAT6 followed by reduction in GATA3 expression.[11]

Atherosclerosis

Atherosclerosis occurs due to the formation of plaque inside the blood vessels leading to thickening of the arteries. An investigation into the effect of AKBA on mice apolipoprotein E-deficiency (ApoE-/-) showed that it inhibited NF-κB, a vital factor element for the development and prognosis of various inflammatory diseases. so, this finding suggests that Boswellia family plant resins may provide a substitute for conventional treatment strategies for chronic inflammatory diseases like atherosclerosis. [12]

Cancer

Cancer is one of the most fatal diseases of humanity, with an extremely high incidence and mortality rate. In 2012, it was estimated that about 14.1 million people suffered the disease and 8.2 million people succumbed to death, while in the year 2018, the number of deaths increased to 9.8 million worldwide. Notably, most of the existing medication have serious side effects and are mainly ineffective to the development of chemo-resistance.[13] This has led to change in attention towards natural products like as Butein, Emodin, Curcumin, Epigallocatechin Gallate (EGCG), Celastrol, Honokiol, Resveratrol, etc. which have shown high potential against various types of cancer. In addition, different studies have shown the efficacy of BA in the prevention and treatment of breast, bladder, cervical, prostate, colorectal, head and neck, liver, lung, and pancreatic cancers, etc.[14]

a) Breast Cancer

In order to explore the potential of 3-O-Acetyl-_-BA (3-OA-α-BA) and B.serrata extract (BSE) in the prognosis and treatment of breast cancer, an in vitro study was performed on MDA-MB-231 cells. Both BSE and 3-OA-α -BA were found to be effective against triple-negative breast cancer by upregulating the expression of PERK-ER/UPR (protein kinase RNA-like endoplasmic reticulum kinase- endoplasmic reticulum/unfolded protein response) pathways that can regulate activated programmed cell death (APCD). Also, BSE and/or 3-OA- α - BA considerably downregulated the expression of oncogenes (OG) and upregulated the expression of tumour suppressor genes (TSGs), which includes glutathione-depleting ChaC glutathione-specific gamma glutamyl cyclotransferase 1 (CHAC1) and the mTOR inhibitors–sestrin 2 (SESN2) Tribbles homolog 3 (TRIB3), homocysteine-inducible, endoplasmic reticulum stress-inducible, ubiquitin-like domain member 1 (HERPUD1), and cystathionine gamma-lyase (CTH).[15]

b) Bladder Cancer

recently, 430,000 people are diagnosed with bladder cancer yearly, and 165,000 people died every year all across the globe.[16] To evaluate the anti-cancer effect of frankincense oil, (main component of which is BA), an in vitro study on J82 (human bladder cancer) and UROtsa cells (immortalized normal bladder urothelial cells) was performed. Treatment with frankincense oil exerted cytotoxic effects on the J82 cell line but had minimal effect on UROtsa cells. Thus, frankincense oil was found to differentiate between cancerous cells and normal cells and caused the suppression of tumour cell viability.[17]

c) Brain Cancer

Almost 256,213 individuals, which include 116,605 females and 139,608 males, in the year 2012, were diagnosed with a primary malignant brain tumour, worldwide. Glaser et al., in 1999, observed that at low micromolar concentrations, BAs showed cytotoxicity against malignant glioma cells. Further, the pure extract of the gum resin of B.serrata and various derivatives of BA including AKBA, BBA, and Cyano Enone Of Methyl Boswellates (CEMB) have shown cytostatic and apoptosis-inducing activity against glioma cells. Studies by Park et al., on meningioma cells also suggested that the cytotoxic action of AKBA might, at least in part, be mediated by Erk signal transduction pathway inhibition. additionally, in vivo studies on an immunocompromised mice model (C6 glioma tumour xenograft) reported that intratumor administration of CEMB significantly inhibited the tumour growth, signifying the potent antitumor effect of CEMB.[18]

d) Cervical Cancer

One of the main reasons for female malignancy in the world is cervical cancer, causing almost 265,700 deaths yearly. In cervical cancer, treatment with 3-α-propionyloxy-β-BA (POBA) caused PARP cleavage, which consequently led to a cell cycle arrest, DNA fragmentation, and loss of mitochondrial membrane potential in SiHa cells.[19]

e) Colon Cancer

The apoptotic and antiproliferative effects of the analogues of BA, such as BBA, KBA, and AKBA in colon cancer cells, were analysed. It was observed that AKBA could induce apoptosis through caspase activation and the p21-dependent pathway. In vitro studies on human colon cancer cells further showed that the potent anticancer effects of BA might be mediated via induction of apoptosis and cell cycle arrest, as well as abrogation of PI3K/Akt signalling pathway.[20] Also, AKBA affected the growth of colorectal cancer cells through genetic (Ki-67 and CD31) and epigenetic modulations (demethylation and miRNA regulation). additionally, AKBA, in combination with curcumin,

showed antitumorigenic effects in vitro and in vivo by regulating specific cancer-related miRNAs such as miR-34a and miR-27a in colorectal cancer cells.[21]

f) Leukaemia

The antitumor activity of BA and its analogues, such as BBA, KBA, AKBA, and PKBA, were studied in deferent leukemic cell lines such as HL-60, K562, MOLT-4, THP-1, CCRF-CEM, ML-1, NB4, SKNO-1, and U937 cells. Results showed that the treatment with BA exerted cytostatic and cytotoxic effects through the induction of apoptosis. Upon examining the molecular mechanisms involved, it was found that the treatment resulted in the attenuation of topoisomerases I and II, the release of cytochrome c, the loss of mitochondrial membrane potential, activation of caspases, and cleavage of PARP. It was also reported that the treatment led to the decreased expression of MMP-1, MMP-2, and MMP-9 mRNAs; along with the secretions of TNF-_ and IL-1_; reduced the phosphorylation of ERK1/2, p38 MAPKs; and disrupted PI3K/AKT/Hsp-90 cascade.[22,23]

g) Liver Cancer

Around 782,500 new cases and 745,500 cancer-related deaths have occurred due to liver cancer or hepatocellular cancer. When the effects of KBA and AKBA were evaluated, they were found to inhibit proliferation and induce apoptosis through the caspase-8-dependent pathway in liver cancer cells.[24] Also, BSE, when administered as monotherapy and in combination therapy with DOX, caused an augmentation in caspase-3 activity, TNF-_, and IL-6 levels, thus showing growth-modulatory and apoptotic actions in hepatocellular carcinoma cells.

g) Lung Cancer

An in vitro study on H446 cells was performed to explore the antitumor potential of 11-carbonyl-BBA. It was found to activate JNK signaling pathway, cause the cleavage of PARP, and down regulate surviving protein expression, thus showing inhibitory effects on lung cancer cells. Moreover, a study focusing on the potential of POBA showed that POBA initiated PARP cleavage on HOP-62 lung cancer cells. As a consequence of the treatment, induction of apoptosis, as well as cell cycle arrest occurred in lung cancer cells.[19]

h) Prostate Cancer

In a study it was reported that prostate cancer accounts for nearly 1.1 million new cases all across the world.[25] AKBA was shown to elicit cell death and reduce cell proliferation in PC-3prostate cancer cell lines by abrogation of the activated NF-_B signaling pathway via interception of I_B kinase activity and activation of caspase-3. In LnCaP and PC-3 prostate cancer cells, AKBA showed apoptotic effects driven by the death receptor 5-mediated pathway. Besides that, caspase-3 and caspase-8 activation, as well as PARP cleavage induction, were evidenced. In another study, AKBA was found responsible for the suppression of VEGFR2-mediated angiogenesis in prostate cancer. Studies by Liu et al., showed that AKBA suppressed docetaxel-resistant prostate cancer cells via blockage of STAT3 and Akt signaling pathways. A semi-synthetic triterpenoid derivative, 3-cinnamoyl-11-keto-beta-BA (C-KβBA), demonstrated specific antiproliferative and proapoptotic effects in cancer cell lines such as PC-3, LnCaP, and DU-145, as well as in PC-3 prostate cancer xenografts, by downregulating the activation of p70 ribosomal S6 kinase.[26]

i) Pancreatic Cancer

Pancreatic cancer is the seventh most leading cause of cancer deaths in the world, and the rate of incidence is parallel to the rate of mortality due to pancreatic cancer. To evaluate the role of AKBA, different in vitro studies on pancreatic cancer cell lines, such as AsPC-1 and PANC-28, and in vivo studies were performed. AKBA was found to inhibit cell growth and down regulate the expressions of Ki-67, CD31, Cox-2, MMP-9, CXCR4, and VEGF in the tumor tissues. Recently, combination of the anti-diabetic drug metformin and BA nanoparticles showed synergism in inhibiting the growth of pancreatic cancer cell.[27]

j) Melanoma

Mainly the population of the world bearing white skin is prone to melanoma,and it is considered as a serious global concern. The effect of an isomeric compound, BC-4, containing both α- and β-BA acetate was studied via in vitro study. It was observed that BC-4 was responsible for the induction of B16F10 cells differentiation, blockage of the cell population in the G1 phase of the cell cycle, attenuation of topoisomerase II activity as well as the migratory potential of B16F10 cells when administered at a concentration of 25_M for 48h. Further, in fibrosarcoma cells, HT-1080 apoptosis was induced, and MMP secretion was reduced after treatment with BA.[28]

k) Renal Intestinal Fibrosis

The role of AKBA in renal-intestinal fibrosis was studied both in vitro and in vivo using hypoxia-induced HK-2 cells and C57BL/6 mice, respectively via unilateral ureteral obstruction (UUO). The findings showed that AKBA exhibited a Reno protective effect via modulation of the Klotho/TGF-β/Smad signalling pathways. Hence, AKBA can be employed selectively for the treatment of renal-intestinal fibrosis.

Inflammatory Bowel Disease

IBDs can be defined as idiopathic chronic relapsing malfunctions of the gastrointestinal tract (GIT) with an unknown origin, is characterized by the befor six weeks improved the stool properties, histopathology, and blood parameters, including Hb, serum iron, calcium, phosphorus, proteins, total leukocytes, and eosinophils. Further, in an attempt to study the effect of AKBA on experimental ileitis, it was observed that treatment with AKBA caused a significant decrease in rolling (up to

90%) and adherent (up to 98%) leukocytes. Also, high doses of Boswellia extract, as well as AKBA, significantly reduced tissue injury scores. Moreover, in an investigation on the effects of BSE in mouse models of chemically induced colitis, it was found that BA was incapable of ameliorating the symptoms of colitis and it exerted hepatotoxicity at higher doses. Contrary to this report, another study demonstrated the anti-inflammatory effect of the semisynthetic form of AKBA and showed that P-selectin-regulated recruitment of inflammatory cells may be a major site of action for this novel anti-inflammatory agent in dextran sodium sulphate (DSS)-induced experimental murine colitis.[29]

Diabetes

Diabetes is becoming the leading causes of death worldwide. It is classified into two types – Type 1 diabetes (T1D) and Type 2 diabetes (T2D). T1D is an autoimmune disorder whereas T2D is a metabolic disorder. A study on alloxan-induced diabetic rats reported significant hypoglycaemic effects on the continued use of the aqueous extract of leaves and roots of Boswellia glabra. Moreover, a decrease in the serum glucose level, cholesterol, triglyceride, urea and creatinine levels, and enzyme activities (alkaline phosphatase and glucose-6-phosphatase) was observed after treatment. Also, it was observed that the administration of BSE can cause a significant decrease in blood glucose level along with HbA1c, cholesterol, LDL, and fructosamine. Like, the isolated compounds from the plant, such as KBA and AKBA prevented the occurrence of autoimmune reactions, insulitis, and reduced hyperglycaemia in multiple low-dose streptozotocin (MLD-STZ)-induced diabetes models.[30]

Central Nervous System Disorders

BAs may also have tremendous potential in the treatment of central nervous system disorders such as Parkinson's, Alzheimer's disease, and cognitive impairment. Treatment with BAs has shown reduced inflammatory markers, improved general motor performance, nigral tyrosine hydroxylase immunostaining, and increased striatal dopamine levels in Parkinsonian rats. The effects of α-BA were investigated in primary fetal human astrocytes under a stress paradigm as a probable model for Alzheimer's disease. The results showed that α-BA could be considered as an effective remedy for prevention and lessening the progression of Alzheimer's hallmarks in astrocytes; though, further preclinical findings are critical. In a neuroinflammatory model of mice, AKBA showed antiapoptotic and anti-amyloidogenic effects via modulation of miRNA-155. Moreover, BA exhibited a neuroprotective role in Wistar rat models of cognitive impairment.[31] In another model of cognitive dysfunction, combination treatment with AKBA and celecoxib exhibited anti-inflammatory, ant glutamatergic, and ant amyloidogenic properties, leading to better prognosis of the disease.

Ischemia-Reperfusion Injury (IRI)

IRI is a physio pathological condition involving numerous metabolic processes which finally leads to cell apoptosis and ultimately tissue necrosis. The protective effect of KBA against myocardial IRI in rats was observed. Three dose levels of KBA exerted dose-dependent cardioprotective effects, as manifested by a dose- dependent drop in serum lactate dehydrogenase and infarct size. In ischemic brain injury also, AKBA was responsible for neuroprotection that involved the Nrf2/HO-1 defense pathway. It was found that the administration of AKBA increased Nrf2 and HO-1 expression, and a similar observation was also made for the compound KBA against cerebral ischemia-reperfusion injury.[32]

Psoriasis

The gum resin of B. serrata has been also found effective in curing diverse skin problems such as psoriasis. A study was conducted to evaluate the effect of AKBA using murine bone marrow-derived dendritic cells (BMDCs) and a psoriasis-like mouse model, respectively. The results confirmed the anti-inflammatory effects of AKBA on psoriasis via modulation of IRF and TLR7/8 signalling pathways.[33]

Other Diseases

Apart from the above-mentioned diseases, a few reports on other diseases are also available where positive effects of BAs have been observed. In a study on guinea pigs with experimental autoimmune encephalomyelitis, BAs were found to reduce the clinical symptoms of the disease. In an attempt to assess the antiulcer properties of BA, it was found to inhibit the ulcer formation in different experimental models. It was suggested that the protective action comes from enhanced gastric mucosal resistance, cytoprotective prostaglandins synthesis, and leukotriene synthesis inhibition. A study on the gastroprotective role of α-BA was performed in ethanol-induced gastric injury in rats. The findings demonstrated that α-BA decreased ethanol administration related injuries, gastric juice acidity, and the development of MDA, and improved CAT activity along with SOD activity and the level of NO and PGE-2. In the case of myocardial injury, AKBA in combination with HSYA showed cardioprotective effects via modulation of the PGC-1α/Nrf2 pathway. In another study, the efficacy of BA against acetaminophen (APAP)-induced hepatotoxicity in Balb/c mice was determined. It was observed that BA pre-intake reduced APAP-induced production of inflammatory cytokines and chemokines. Further, it affected the expression of NF-κB p65 and p-JNK, TLR-3, TLR-4, and MyD88.

BIOAVAILABILITY OF BOSWELLIC ACIDS

Among six most important derivatives of Boswellic acids, KBA and AKBA are the most potent inhibitors of 5-lipoxygenase. Low water insolubility and extensive phase I metabolism are the main limiting factors,

responsible for low metabolic stability of KBA and AKBA.

Preliminary pharmacokinetic studies BY Sterk et al revealed very low conc. of KBA in human plasma after oral administration of *Boswellia serrata* extract. Further studies revealed that about 80% of initial conc. of KBA is metabolized after 15 min and less than 1% of starting conc. is remained after 120 min. But this was not observed in case of AKBA whose starting conc. still remained approximately same after 120 min. The above described metabolic behaviour of KBA and AKBA is due to extensive hepatic phase I metabolism. A further reason for the lower plasma levels of AKBA compared with KBA might be greater volume of distribution of AKBA associated with its greater lipophilicity. To overcome these limitations many approaches have been investigated including synthetic analogues, combined with other dietary components, using nanoscale drug delivery systems. Among these methods, nanoscale drug delivery systems have become main alternatives for many researchers as a potential area to develop new formulations of therapeutically bioactive components. Many successful attempts of combination of nanotechnology and traditional medicine have been made in the past using other targets.

Consequently, a good understanding of nanotechnologies is necessary for the advancement of BAs with higher efficacy. Till date many studies have focused on loading BAs into liposomes or nanoparticles, forming solid lipid nanoparticles and much progress has been made in the past ten years. The purpose of this review is to provide an updated summary of the applications of novel delivery systems of BAs, so that further strategy can be planned.

SUMMARY AND CONCLUSION

Boswellia species has been used in traditional and modern natural medicine for the treatment of variety of variety of illness with very minimal side effects. Boswellic acids, the pentacyclic triterpenic acids comprising of α-,β-,γ-Acetyl-β-BA,KBA,AKBA, and so on. They can target several key players involved in the pathogenesis of chronic diseases like inflammatory disorders, asthma, various cancer, rheumatoid arthritis, inflammatory bowel diseases, heart disease etc. it was observed that different important molecular targets are affected by BA treatment, such as LO, MAPK, NF-κ, TNF-α etc. BA help to produce anti-inflammatory, anti-arthritic, anti-proliferative, anti-microbial and analgesic effects. The action of Boswellia remarkable in increasing the number of dendritic segments and branching in the neuron cells of hippocampus, causing more synaptic connections in that area and, therefore, improvement of learning and memory. extensive studies on Boswellia and its effect on neurophysiology could be a right approach in finding a possible new complementary or alternative natural medicine to control, cure, or prevent some kinds of neurodegenerative diseases such as Parkinson's and Alzheimer's.

Development of novel delivery systems of Bas with better curative effect will be critical for future development of Bas as a therapeutic agent. Elaborated studies are taking place on Liposome, Phytosome, Niosome, Nano- particles and microsphere formulations.

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