

Natural Anti-Inflammatory Agents from *Salvia hispanica* and *Buxus papillosa*: Targeting NF- κ B, MAPK, and JAK-STAT Signaling Pathways

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ABSTRACT

Inflammation is a complex biological response of the immune system to harmful stimuli such as pathogens, tissue injury, chemical irritants, and oxidative stress. While acute inflammation plays a protective role by eliminating injurious agents and initiate tissue repair, persistent or uncontrolled inflammation may lead to chronic inflammatory disorder. The inflammatory process involves the coordinate activation of immune cells, cytokines, enzymes, and intracellular signaling pathways such as nuclear factor kappa-B (NF- κ B), mitogen-activated protein kinase (MAPK), and Janus kinase–signal transducer and activator of transcription (JAK-STAT).

The growing concern over adverse effects associated with synthetic antiinflammatory drugs has shifted research toward natural plantbased therapeutics. This review presents a detailed overview of cellular and molecular mechanism of inflammation. In addition, the phytochemical composition and anti-inflammatory potential of *Salvia hispanica* L.(chia seeds) and *Buxus papillosa* have been critically discussed.

Salvia hispanica L. is a rich source of omega-3 fatty acid, flavonoid, phenolic acids, and anti oxidants, which exert anti inflammatory effects by inhibiting pro inflammatory cytokines and modulating NF- κ B and MAPK signaling pathways. Similarly, *Buxus papillosa* contains diverse bio-active constituents such as steroidal alkaloids, triterpenoids, flavonoid and alkaloids that shows anti-inflammatory activity through suppression of inflammatory mediators and oxidative stress

Overall, this review highlight the therapeutic relevance of *Salvia hispanica* L. and *Buxus papillosa* as natural source for the development of safer and effective plant based anti inflammatory agents, supporting their potential use as alternative in inflammation related disorders.

Keywords: Inflammation, Anti-inflammatory activitiy, *Salvia hispanica*, Chia seeds, *Buxus papillosa*, Shamshad, ;Phytochemicals, Omega-3 fatty acids, Flavonoids; Alkaloids, Triterpenoids; NF- κ B pathway, MAPK pathway, JAK-STAT signaling, Oxidative stress, Natural anti-inflammatory agents

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INRODUCTION

Inflammation is immune system's reaction to adverse stimuli, such as pathogens, damaged cells, poisonous substances, or radiation [1], which operates by eliminating harmful stimuli and starting inflammation serves as a the healing process [2]. This protective mechanism that is essential for maintaining health [3].

Cellular and molecular events interactions in most cases effectively reduce impending damage or infection during acute inflammatory reactions. This mechanism of mitigation helps to resolve the acute inflammation and restore tissue homeostasis. But unchecked acute inflammation can develop into chronic inflammation, which can lead to a number of chronic inflammatory disorders [4].

Inflammation at the tissue level is marked by redness, swelling, warmth, discomfort, and impaired tissue function. These symptoms arise from localized immune, vascular, and inflammatory cell reactions to infection or harm [5]. Different disease-causing factors, like

infection, tissue damage, or heart attack, can trigger inflammation by causing harm to tissues. The origins of inflammation can be either infectious or non-infectious (Table 1).

Table 1: Etiology of inflammation

Non - infectious factor	
Physical	Burn, frostbite, physical injury, foreign bodies, trauma, ionizing radiation
Chemical	Glucose, fatty acid, toxins, alcohol, chemical irritants (including fluoride, nickel and other trace element)
Biological	Damaged cells
Psychological	Excitement, stress, anxiety, depression
Infectious factor	
Bacteria	Mycobacterium tuberculosis
Viruses	Hepatitis virus
Other microorganism	fungi

INFLAMMATORY RESPONSE MECHANISMS

The inflammatory response is the coordinate activation of signalling pathways that regulate inflammatory mediator levels in resident tissue cells and inflammatory cells recruited from the blood [8]. Chronic diseases such as cardiovascular bowel diseases, diabetes, arthritis, and cancer have inflammation as common pathogenesis [9].

Pattern recognition receptor activation

Pathogen-associated molecular patterns (PAMPs), which are microbial structures, have the ability to start the inflammatory response. They do this by turning on pattern recognition receptors (PRRs). These receptors are encoded in the germ line and appear in immune and non-immune cells [10, 11]. Some PRRs also spot different signals from inside the body that become active when tissue or cells are hurt. These are known as danger-associated molecular patterns (DAMPs) [11]. DAMPs are bio molecules from the host that can start and keep going an inflammatory response that is not caused by infection [12]. When cells are broken, they can also innate inflammatory cells even when there are no pathogens present, by releasing DAMPs [13]. The Toll-like receptors (TLRs), C-type lectin receptors (CLRs), retinoic acid inducible gene (RIG)-I-like receptors (RLRs), and NOD-like receptors (NLRs) are groups of PRR families [5]. TLRs are a group of mammalian PRRs that are highly conserved and help to activate the inflammatory response [14].

TLRs are the most thoroughly researched of the known PRRs, with over 10 members of the TLR family found [15]. Myeloid differentiation factor-88 (MyD88) and TLRs mediate the transmission of PAMPs and DAMPs. TLR signalling triggers an intracellular signalling cascade [16,17] that causes transcription factors including activator protein-1 (AP-1), NF- κ B, or interferon regulatory factor 3 (IRF3) to translocate into the nucleus. Similarities between infectious and non infectious inflammatory responses are suggested by the fact that DAMPs and PAMPs share receptors such TLR4 [18, 19].

Activation of inflammatory pathways

Pathway of inflammation effect the pathogenesis of many chronic disease and include many familiar inflammatory mediators and regulatory pathways .The triggering of inflammation-related routes affects the development of various long-term illnesses, involving shared inflammatory substances and control mechanisms. Inflammatory triggers turn on internal signalling routes that then stimulate the creation of inflammatory mediators. Key inflammatory stimuli, such as microbial by products and cytokines like interleukin-1 β (IL-1 β), interleukin-6 (IL-6), and tumour necrosis factor α (TNF- α), facilitate inflammation by engaging with the TLRs, IL-1 receptor (IL-1R), IL-6 receptor (IL-6R), and the TNF receptor (TNFR) [20]. Receptor stimulation sets off significant internal signaling routes, including the mitogen-activated protein kinase (MAPK), nuclear factor kappa-B (NF- κ B), and

Janus kinase (JAK)- signal transducer and activator of transcription (STAT) pathways [21–23].

NF- κ B pathway

The NF- κ B transcription factor is crucial in processes like inflammation, immune reactions, survival, and programmed cell death [24]. The NF- κ B group consists of five linked transcription factors: P50, p52, RelA (p65), RelB, and c-Rel [25,26]. NF κ B function is triggered by various stimuli, such as substances from pathogens, inflammatory cytokines between cells, and numerous enzymes [27,28]. In normal conditions, I κ B proteins found in the cytoplasm suppress NF- κ B [29]. PRRs employ comparable signal transduction methods to activate I κ B kinase (IKK), which contains two kinase subunits, IKK α and IKK β , along with a regulatory subunit like IKK γ . IKK controls NF- κ B pathway activation via I κ B phosphorylation [8]. I κ B phosphorylation leads to its breakdown by the proteasome and the subsequent freeing of NF- κ B for movement to the nucleus and activation of gene transcription [30].

MAPK pathway

MAPKs represent a group of serine/threonine protein kinase that control cellular reactions to diverse signals, like osmotic pressure, mitogens, heat exposure, and inflammatory cytokines (such as IL-1, TNF- α , and IL-6). These signals modulate cell growth, specialization, cell survival, and programmed cell death [31, 32]. The MAPKs in mammals encompass extracellular-signal-regulated kinase ERK1/2, p38 MAP Kinase, and c-Jun N-terminal kinases (JNK) [33]. Every MAPK signaling route involves a minimum of three parts: a MAPK, a MAPK kinase (MAPKK), and a MAPK kinase kinase (MAPKKK). MAPKKKs phosphorylate and trigger MAPKKs, which then phosphorylate and trigger MAPKs [33,34]. ERKs are commonly triggered by mitogens and signals for specialization, whereas stress and inflammatory signals trigger JNK and p38 [35]. MKK1 and MKK2 trigger ERK1/2, MKK4 and MKK7 trigger JNK, and MKK3 and MKK6 trigger p38. Triggering of the MAPKs, including Erk1/2, JNK, results in phosphorylation and activation of p38 transcription factors present in the cytoplasm or nucleus, which starts the inflammatory reaction [32, 36].

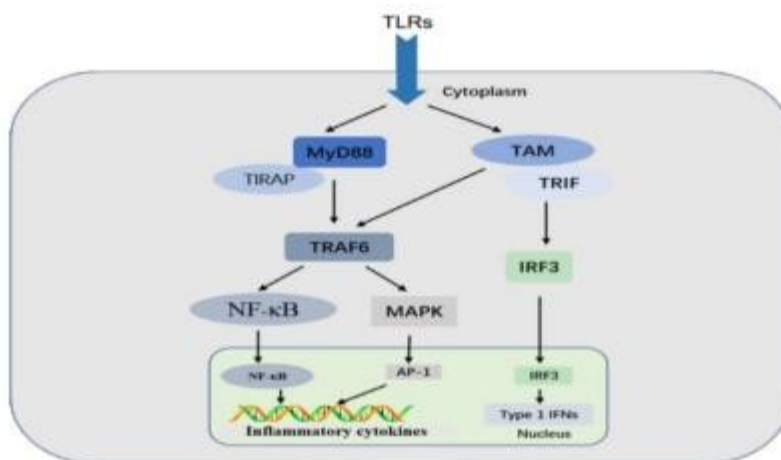


Figure 1: TLR signaling. MyD88-dependent and TRIF-dependent pathways are shown. Signaling through TLRs activates intracellular signaling cascades that lead to nuclear translocation of AP-1 and NF- κ B or IRF3, which regulates the inflammatory response.

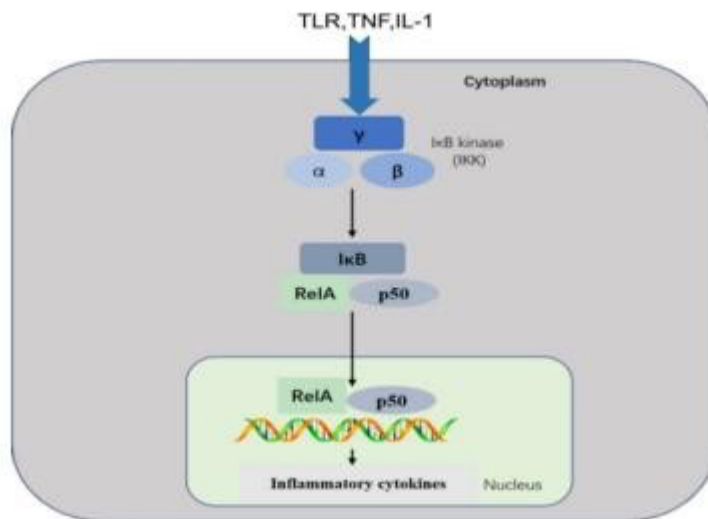


Figure 2: NF- κ B pathway. This pathway is triggered by TLRs and inflammatory cytokines, such as TNF and IL-1, leading to activation of RelA/p50 complexes that regulate expression of inflammatory cytokines. NF- κ B signaling requires IKK subunits, which regulate pathway activation through I κ B phosphorylation.

JAK-STAT pathway

The well-preserved JAK-STAT route includes various cytokines, growth elements, interferons, and similar compounds, like leptin and growth hormone. It acts as a signaling method through which external elements influence gene activity [37]. Receptor-linked JAKs are triggered by ligands and phosphorylate each other, forming binding locations for STATs, which are inactive transcription factors located in the cytoplasm. Cytoplasmic STATs drawn to these spots experience phosphorylation and then dimerization before moving to the nucleus [38]. Tyrosine phosphorylation is crucial for STAT dimerization and DNA attachment [39]. Thus, JAK/STAT signaling enables the immediate conversion of an external signal into a transcriptional reaction. As an illustration, the connection of IL-6 family members to plasma membrane receptors activates the JAK-STAT proteins. STAT proteins moved into the nucleus connect to target gene promoter areas to oversee the transcription of inflammatory genes [40].

Inflammatory markers

In clinical settings, markers help distinguish between healthy and diseased biological functions and evaluate how well treatments are working. Inflammatory markers can suggest the presence of inflammatory conditions [41–46] and are linked to the origins and effects of different inflammatory diseases, like heart issues, endothelial problems, and infections [47, 48]. Certain triggers activate inflammatory cells, such as macrophages and fat cells, leading to the creation of inflammatory cytokines like IL1 β , IL-6, TNF- α , and various inflammatory proteins and enzymes. These substances could be useful as biomarkers for disease

diagnosis, prediction, and guiding treatment choices [49–53].

Inflammatory cytokines

Immune cells such as monocytes, macrophages, and lymphocytes are the main sources of cytokines. Inflammation is facilitated by pro-inflammatory cytokines and inhibited by anti-inflammatory ones. Cells produce inflammatory cytokines, which include ILs, colony stimulating factors (CSF), IFNs, TNFs, TGFs, and chemokines, mainly to attract leukocytes to the site of infection or injury [54]. Through a complex web of interactions, cytokines control inflammation and the immune response to infection or inflammation. On the other hand, overproduction of inflammatory cytokines can cause organ failure, hemodynamic abnormalities, tissue damage, and eventually death [55, 56]. Treating inflammatory illnesses and accurately identifying agent-mediated inflammation would be made possible by a better understanding of how to control cytokine pathways [54].

Inflammatory proteins and enzymes

During injury, stress, or infection, inflammatory proteins present in the bloodstream, such as C-reactive protein (CRP), haptoglobin, serum amyloid A, fibrinogen, and alpha 1-acid glycoprotein [57], aid in re-establishing balance and limiting microbial proliferation without the need for antibodies [58]. Irregular activation of particular enzymes, including high-mobility group box 1 (HMGB1), superoxide dismutase (SOD), glutathione peroxidase (GPx), NADPH oxidase (NOX), inducible nitric oxide synthase (iNOS) and cyclooxygenase (COX)-2, are important in the emergence of diseases linked to inflammation, like heart disease and cancer

[59–62]. As an illustration, the effects of extracellular HMGB1 can be influenced by the stimulation of TLR-coupled signaling pathways [63]. The main focus of extracellular HMGB1 is TLR4 [64], which sets off MyD88-reliant intracellular signaling pathways involved in activating the NF- κ B and MAPK pathways. This results in the discharge of inflammatory cytokines such as TNF- α and IL-1 β [63]. In the medical field, inflammatory proteins and enzymes have been utilized as biomarkers for inflammation, infection, and trauma.

Other inflammatory markers

Antioxidant defense mechanisms, such as antioxidant enzymes, affect oxidative stress.

Increased oxidative stress may result in the production of reactive oxygen species (ROS), malondialdehyde (MDA), 8-Hydroxy-2-deoxyguanosine (8-OHdG), and isoprostanes [60, 65], all of which are capable of activating different transcription factors, like NF- κ B, AP-1, p53, and STAT. Consequently, this sequence can enhance the expression of genes that encode growth factors, inflammatory cytokines, and chemokines [66]. Oxidative stress is linked to the development of numerous diseases, including heart disease, cancer, diabetes, high blood pressure, aging, and atherosclerosis. As a result, oxidative stress byproducts can also serve as indicators of the inflammatory reaction.

Cell types in inflammatory responses

The inflammatory reaction requires a well-organized system involving various cell types. Stimulated macrophages, monocytes, and other cells facilitate local reactions to tissue harm and infection. In areas of tissue injury, compromised epithelial and endothelial cells secrete elements that initiate the inflammatory sequence, along with chemokines and growth factors, which draw

in neutrophils and monocytes. The initial cells drawn to an injury site are neutrophils, then monocytes, lymphocytes (natural killer cells [NK cells], T cells, and B cells), and mast cells [67–69]. Monocytes have the capacity to develop into macrophages and dendritic cells and are drawn into injured tissues through chemotaxis. Immune cell changes caused by inflammation are linked to numerous conditions, such as asthma, cancer, long-lasting inflammatory conditions, atherosclerosis, diabetes, and autoimmune and weakening conditions. Neutrophils, which aim at microorganisms in the body, can also harm host cells and tissues [70].

Salvia hispanica

Chia seed, or *Salvia hispanica* L., is an annual herbaceous plant that is native to Northern Guatemala and Southern Mexico. It is a member of the genus *Salvia*, subfamily Nepetoideae, mint family Labiate, and order Lamiales. For thousands of years, the about 900 species that make up the genus *Salvia* have been widely dispersed throughout many parts of the planet, including Southern Africa, Central America, North and South America, and South-East Asia [71–78]. According to the literature, chia is now grown in Australia, Bolivia, Columbia, Peru, Argentina, America, and Europe in addition to Mexico and Guatemala. Mexico is currently acknowledged as the world's top producer of chia [72].

Salvia hispanica L. is mainly cultivated for its seeds and produces bisexual, white and violet flowers that range from 3 to 4 mm in diameter. The plant can grow up to one meter tall, possesses inversely petiolate, toothed leaves that measure 4 to 8 cm in length and 3 to 5 cm in width, and is affected by the amount of sunlight. Generally, chia seeds have an oval form, a length of 2 mm, a width of 1 to 1.5 mm, and a thickness of less than 1 mm [72,75,76,79].



Figure 3: chia seeds [80]

Phytochemicals in chia seeds

Chia seeds are rich in fats (30–33%), carbohydrates (26–41%), dietary fiber (18–30%), proteins (15–25%), as well as vitamins, minerals, and antioxidants (on a wet basis), as illustrated in Figure 1. The nutritional composition of chia seeds per 100 g, according to the

USDA's National Nutrient Database [81], is presented in Table 2 and Table 3, along with a comparison to other common grains. Numerous studies have examined the phytochemicals in chia seeds, with findings emphasizing that the primary components of chia oil are polyunsaturated fatty acids (PUFAs), specifically α -

linolenic acid (ALA, an ω -3 fatty acid) and linoleic acid (LA, an ω -6 fatty acid) [82]. Chia seeds have a 39% oil content (based on dry seed mass), which is composed of up to 68% ω -3 and 19% ω -6 fatty acids [71,75].

Table 2: Basic composition of chia seeds [19].

Sr. no.	Nutrients	Content of nutrients
1.	Fats	30-33%
2.	Carbohydrates	26-41%
3.	Dietary fibers	18-30%
4.	Proteins	15-25%

Table 3: Active compounds in Chia seeds.

Sr. no.	Active compound	Biological activity	Reference
1.	Omega-3 fatty acid, ω -3 fatty acid, ω -3ALA	Anti-inflammatory, antidiabetic, anticancer	76
2.	Omega-6 fatty acid, ω -6 fatty acid, ω -6 ALA	Anti-inflammatory, anticancer	76
3.	Mycertin	Antioxidant	76,77,83
4.	Quercetin	Antioxidant, anti-cancerogenic, anti-hypertensive	77,76,83
5.	Kaempferol	Antioxidant	76,77
6.	Caffeic acid	Antioxidant, anti-cancerogenic, anti-hypertensive	77,83,84
7.	Rosmarinic acid	Antioxidant	77,83,84
8.	Chlorogenic acid	Antioxidant, anti-cancerogenic, anti-hypertensive	83
9.	Vitamins	Healthy skin, for synthesizing ATP, for normal RBC working	83

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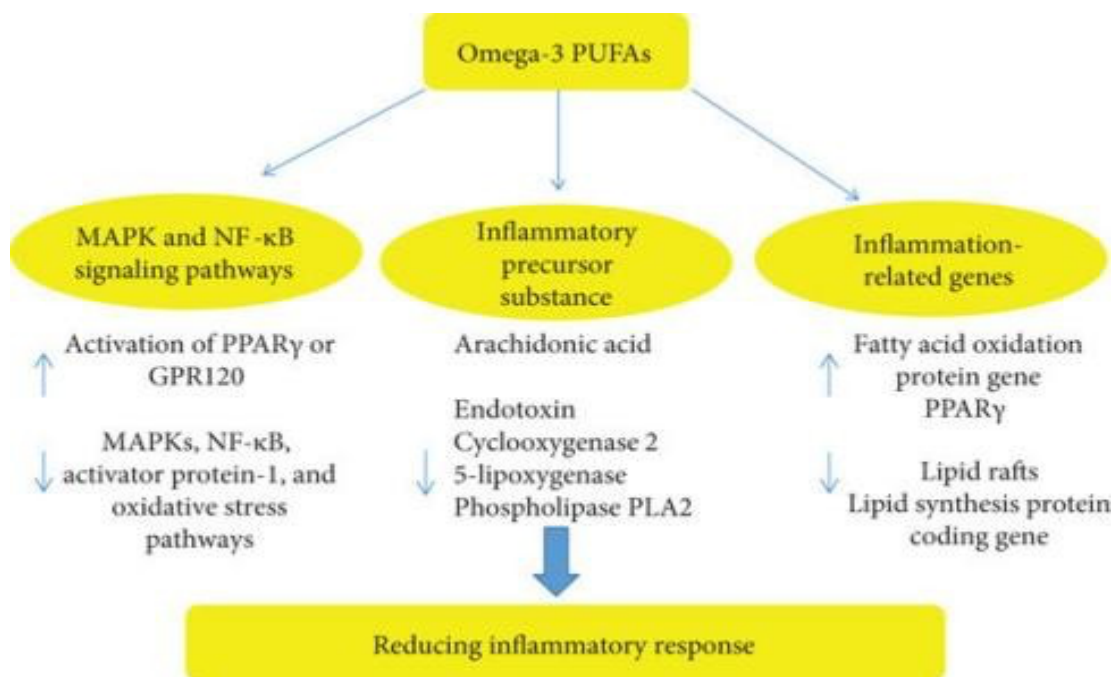


Figure 4: Moa of omega-3 as Active compound in *salvia hispanica* L. seeds [85]

Buxus Pepillosa

About 70 different species of the genus *Buxus*, sometimes known as boxwood, are native to Mexico, Asia, Africa, Madagascar, northern America, the Caribbean, Europe, Cuba, China, and Eurasia, including Turkey and Pakistan. Known as the genus of evergreen shrubs, it is a member of the Buxaceae family [86, 87, 88]. Among other phytochemicals, steroidal, alkaloidal, and triterpenoidal derivatives are most frequently found in the majority of this genus' species [89, 90 91]. Several of these phytochemicals are primarily used in traditional medicine to treat heart problems, malaria, skin issues, cancer, rheumatism, HIV, depression, and exhaustion.[92, 93, 94].*Buxus papillosa*,

often known as a compact, dense evergreen shrub. This plant is found in Pakistan's northern and Himalayan regions. Shamshad is the popular name for *B. papillosa*.

Traditionally, the various portions of this plant have been used to cure rheumatism, headaches, skin conditions, and malaria. They are also thought to be effective antidiarrheal, antisecretory, cardiotoxic, and neurotonic agents [95]. Similarly, there are numerous traditional uses for the various crude extracts of this shrubby plant to treat various ailments, primarily skin infections, rheumatism, and malaria [96]. The entire *B. papillosa* plant has also been used as a diaphoretic, purgative, and antirheumatic agent [97].



Figure 5: *Buxus papillosa* [98]

Phytochemicals of *Buxus Papillosa*

Phytochemicals, often referred to as secondary metabolites, are widely present in plants and are being used as the mainstay for the development of novel therapeutic leads due to their enormous pharmacological effects [99]. The tentative secondary metabolites composition of stem-DCM extract as conducted by UHPLC-MS analysis is presented in Table 4, has revealed the tentative presence of a total of 32 phytocompounds. As presented in Table 2, most of these phytocompounds were belonging to alkaloid and flavonoid groups of secondary metabolites. The

alkaloids tentatively detected were 14,19-dihydroaspidospermatine, prosopinine, uplandicine, cyclobuxine D, cyclovirobuxine C, terminaline, solanocapsine, evocarpine, prosopinine and camptothecin, whereas, the flavonoids were chryso splenside D, melisimplexin, wightin, 8-methoxycirsilineol, dalpaniculin and melisimplexin. Likewise, the other compounds identified were belonging to triterpene/triterpenoid, organic acid, phloroglucinol, polyacetylenic, phenol, carotenoid, vitamin, sesquiterpenoid and vitamin derivatives [100].

Table 4: UHPLC-MS identified compounds of *B. papillosa* stem DCM extract [100].

Sr. no.	Tentative identification (Negative Ionization)	Compound Class
1	Citric acid	Organic acid
2	Suberic acid	Organic acid
3	Chrysoeriol-6-C-glucoside D	Flavonoid
4	Melisimplexin	Flavonoid
5	22-Angeloyltheaspogenol A	Triterpenoid
6	14,19-Dihydroaspidospermatine	Alkaloid

7	Prosopinine	Alkaloid
8	Wightin	Flavonoid
9	8-Methoxycirsilineol	Flavonoid
10	Uplandine	Alkaloid
11	Arjunolic acid	Triterpenoid
12	Lucidumol A	Triterpenoid
13	Quillaic acid	Triterpenoid
Sr. no.	Tentative identification (Positive Ioniization)	Compound Class
14	Cyclobuxine D	Alkaloid
19	Solanocapsine	Alkaloid
20	Dalpaniculin	Flavonoid
21	Evocarpine	Alkaloid
22	Panaxydol linoleate	Polyacetylene derivative
23	Melisimplexin	Flavonoid
24	4-Ketolutein D	Carotenoid
25	Xestoaminol C	vitamin
26	Prosopinine	Alkaloid
27	Wightin	Flavonoid
28	Hemanthidine	Alkaloid

29	8-Methoxycirsilineol	Flavonoid
30	Ermonitin A	Sesquiterpenoid
31	Camptothecin	Alkaloid
32	Pheophorbide A	Chlorophyll derivatives

Atta-ur-Rahman's study team has thoroughly examined the phytochemicals in the *B. papillosa* plant. From this plant, they extracted over 64 steroidal chemicals. Triterpenoidal alkaloids and steroidal alkaloids are among the identified substances.

Table 5 lists the chemicals that were isolated from the various sections of *B. papillosa*. Plants contain a large

number of phytochemicals, often referred to as secondary metabolites, which have enormous pharmacological effects and are currently used as the mainstay for the development of new therapeutic leads [99]. More than 64 steroidal chemicals were extracted from this plant. Triterpenoidal alkaloids and steroidal alkaloids are among the identified chemicals

Table 5: List of isolated compounds from different parts of *B. papillosa*.

<u>Sr. no.</u>	<u>Isolated compound</u>	<u>Part</u>	<u>Reference</u>
<u>Alkaloid steroid</u>			
<u>1</u>	<u>(-)-Cyclobuxupaline-C</u>	<u>Leaves</u>	<u>101</u>
<u>2</u>	<u>(+)-Cyclopapilosine-D</u>	<u>Leaves</u>	<u>101</u>
<u>3</u>	<u>(+)-Buxamine-C</u>	<u>Leaves</u>	<u>101</u>
4	Desoxy-16-buxidienine	Leaves	101
5	Buxaminol-G	Leaves	102
6	Buxaminone	Leaves	103
7	(+)-Buxabenzacine	Leaves	104
8	(+)-Buxafiiranamide	Leaves	104
9	Cyclobuxoviricine	Leaves	105
10	(+)-Buxabenzamidine	Leaves	106
11	(+)-Homobuxaquamarine	Leaves	106
12	(+)-Norcyclocmicrobuxeine	Leaves	106
13	(+)-Buxupapine	Leaves	106
14	(+)-Nb -Norbuxupapine	Leaves	106
15	Cyclobuxoviridine	Leaves	106

16	Cyclohexobuxoviricine	Leaves	107
17	Buxaminol B	Leaves	107
18	(+)-N-Formylharappamine	Leaves	108
19	(+)-N-Formylpapilicine	Leaves	108
20	(-)-Buxoxybenzamine	Leaves	109
21	Papilinine	Leaves	110
22	Papilamine	Leaves	111
23	Papilicine	Leaves	112
24	Moenjodaramine	Leaves	113
25	Harappamine	Leaves	113
26	Karachicine	Leaves	114
27	30-Acetoxy-Na -benzoylbuxidienine	Leaves	115
28	(+)-N-Acetyl-Ndemethylcyclohexobuxeine	Leaves	116
29	(+)-Buxaprogesterone	Leaves	117
30	(-)-Buxapapinolamine	Leaves	117
31	(-)-E-Cyclobuxaphylamine	Leaves	117
32	(-)-Z-Cyclobuxaphylamine	Leaves	117
33	(+)-N-Benzoylcyclohexobuxine-F	Leaves	117
34	N-Tigloylbuxahyrcanine	Leaves	118
35	N-Isobutyrylbuxahyrcanine	Leaves	118
36	Benzoylbuxahyrcanine	Leaves	118
37	Hyrcanol	Leaves	118
38	Hyrcanone	Leaves	118
39	Buxabenzacinine	Leaves	118
40	Buxidine	Leaves	118
41	Buxandrine	Leaves	118
42	Nb -Dimethylcyclohexobuxoviricine	Leaves	118

43	Cyclomicrobuxine	Leaves	118
44	Cyclomicrobuxinine	Leaves	118
45	(+) Papillotrienine	R oots	119
46	(+)-Nb -Demethylpapillotrienine	Roots	119
47	(+)-Nb -Demethylharappamine	R oots	119

48	(-)-Cyclobuxovramme	Leaves	120
Triterpenoid Alkaloid			
49	Buxakashmiramine	Leaves	121
50	Buxakarachiamine	Leaves	121
51	Buxahejramine	Leaves	121
52	Cycloprotobuxine-C	Leaves	121
53	Cyclovirobuxine-A	Leaves	121
54	Cyclomicrophylline-A	Leaves	121
55	Semperviraminol	Leaves	121
56	(+)-N a , N b -Dimethylbuxupapine	Leaves	122
57	(+)-16a-Hydroxypapillamidine	Leaves	122
58	Buxapapillosin	Roots	123
59	11a-Hydroxybuxatenone	Roots	124
60	Buxahejrine	Roots	124
61	(+)-Buxapentalactone	Roots	125
62	(+)-Buxaheptalactone	Roots	125
63	(+)- 3-Deoxybuxandonine	Roots	125
64	(-)-Buxatenone	Roots	126

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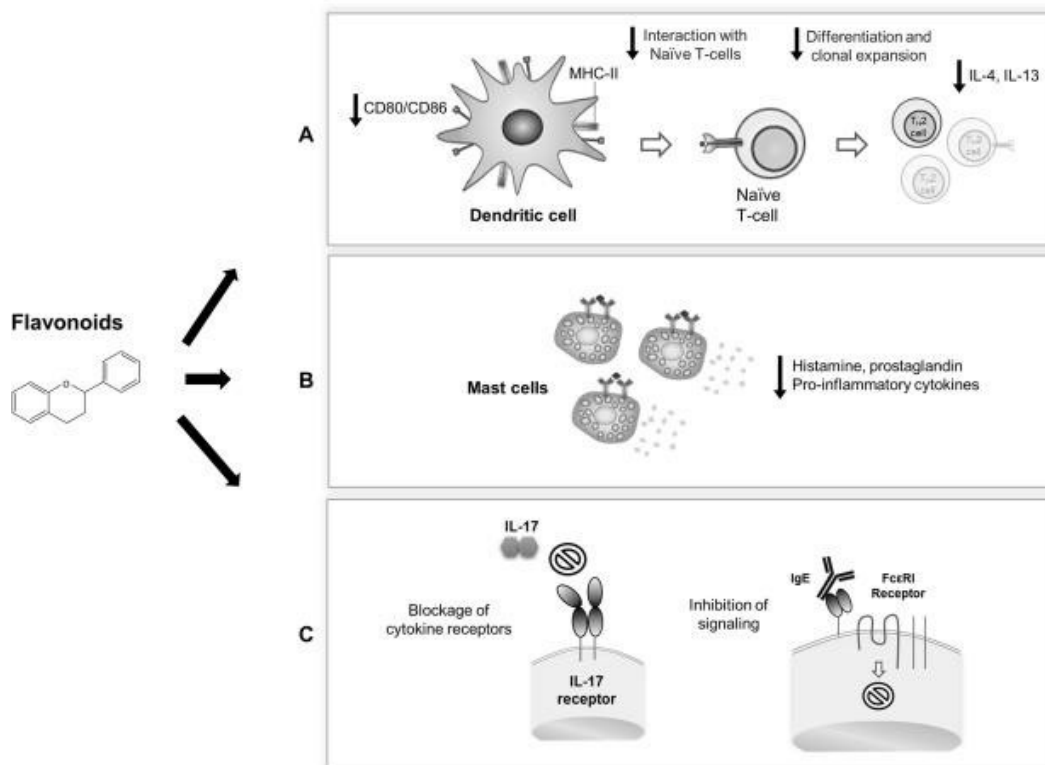


Figure 6: Moa of flavanoid as active compound of *Buxus papillosa* [127].

CONCLUSION

This review highlights the crucial role of inflammation in the pathogenesis of various chronic diseases and emphasizes the potential of natural products as safer antiinflammatory agents. *Salvia hispanica* (chia seeds) and *Buxus papillosa* are rich source of bioactive phytochemical such as omega-3 fatty acid, flavonoids, alkaloids,

And triterpenoids, which exhibit significant antiinflammatory and antioxidant activities. Their ability to modulate key inflammatory pathways NF- κ B, MAPAK, and JAK-STAT, support their therapeutic relevance.

Overall, these plants represent promising candidate for the development of novel plant based anti-inflammatory therapies and indicating their value as natural alternatives or complementary agents in inflammation related disorder.

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