Anti-inflammatory Activity of Medicinal Plants: Present Status and Future Perspectives

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Abstract

Inflammation, a kind of innate immunity, is a biological response of body tissues towards various harmful stimuli. It is known to be initiated as a normal body defense mechanism during injury, exposure to contaminants, radioactive substances, toxicants as well as allergens and infection by a plethora of agents like microbes, viruses. Inflammation is involved in a host of diseases like rheumatoid arthritis, atherosclerosis, obesity, and even cancer. Several inflammatory mediators are produced and secreted at the time of inflammatory responses of different kinds (interferons, interleukins, and tumor necrosis factor-α). Inflammation is associated with the characteristics like pain, swelling, redness, loss of function in the affected area and heat accumulation in the inflamed area. A significant role in human health is being played by natural products with respect to preventing and treating inflammatory conditions. Besides various synthetic anti-inflammatory agents (non-steroidal anti-inflammatory drugs (NSAIDs)) available, herbal medicine still plays a major role to cure various health conditions as large number of medicinal plants possess secondary compounds that retard the key steps of the inflammation pathway (the nuclear factor NF-κβ, lipoxygenase and cyclooxygenase). In addition, many of them exhibit excellent free radical scavenging properties. Many studies have reported about the potential role of herbal medicines in suspending inflammation. This communication summarizes the published literature regarding the anti-inflammatory activities of plant extracts, essential oils, and plant-derived compounds along with the underlying molecular mechanisms of their role in inflammation-mediated metabolic diseases. The huge range of research as well as review papers that have reported about the anti-inflammatory effects of essential oils, plant extracts,

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and/or pure compounds derived from natural products has also been summarized in this chapter. Moreover, this chapter also presents some latest data on some traditionally used medicinal plants that were not investigated yet in this respect.

Keywords

Anti-inflammatory · Anti-oxidants · Reactive oxygen species · Inflammation · Immune cells

Abbreviations

NSAIDs	Non-steroidal anti-inflammatory drugs
NO	Nitric oxide

4.1 Introduction

Inflammation is a pervasive process which occurs in the disturbed state of homeostasis-like injury, subjection to contaminating agents, and infection, the process being activated by the receptors of innate immune system for the elimination of pathogens upon their recognition (de Melo et al. 2014). Inflammation is a defensive mechanism in which both the innate and the acquired immune responses are involved having pain, swelling, redness, heat, and loss of function in the affected area, which is because of dilated blood vessels, and increased spaces between the cells, and thereby resulting in the movement of proteins, leukocytes, and fluids into the regions of inflammation (Fig. 4.1) (Leelaprakash and Dass 2011; Artis and Spits 2015; Azab et al. 2016a, b). The process of inflammation is activated once the body is subjected to lasting shock because of either exogenous or endogenous stimuli such as infectious pathogens, extreme temperature, physical force, irradiation, and irritants (Nathan 2002). During inflammation, a local accumulation of end products (inflammatory mediators) having small molecular weight occurs, which results in the marked increase of the osmotic pressure of the affected tissues along with the aggregation of fluid in excess amount along with raised temperature (Stankov 2012). The synthesis and the secretion of various inflammatory mediators occur during inflammatory reactions of various kinds (Vignali and Kuchroo 2012). Usually, the inflammatory reactions get triggered when immune cells such as neutrophils, dendritic cells and macrophages are activated due to the phagocytosis of pathogens by receptors such as toll-like receptors (TLRs), which are associated with the recognition of molecular patterns of pathogen-derived materials like lipopolysaccharide (LPS) (Hiraiwa and van Eeden 2013).

The inflammatory substances have been categorized as the pro and anti-inflammatory mediators, except for some mediators such as IL-12 (interleukin) that has both pro and anti-inflammatory properties (Vignali and Kuchroo 2012). Several studies associated with human pathological conditions have been carried out studying the inflammatory mediators and cellular pathways such as cytokines (e.g.,

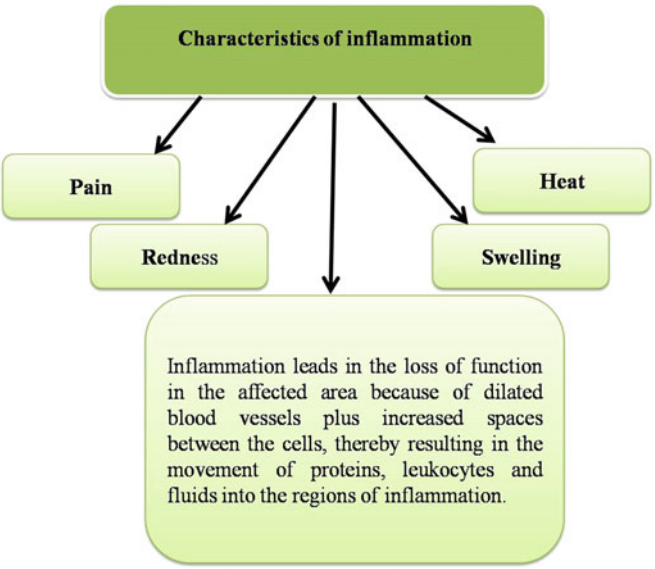


Fig. 4.1 Characteristics of inflammation

interferons, interleukins, and tumor necrosis factor-α), chemokines (e.g., monocyte chemo attractant protein-1), eicosanoids (e.g., prostaglandins and leukotrienes) and the potent inflammation-modulating transcription factor nuclear factor (NF)-κβ (Azab et al. 2016a, b). When the inflammatory cells get activated, they result in elevated intracellular signaling by cascades that involve tyrosine kinases and inhibitor of κβ kinase (IKK), thereby, resulting in activation of the nuclear transcription factor-κβ and stimulated expression of several inflammatory genes like inducible nitric oxide synthase and cyclooxygenase-2 (Byeon et al. 2012; Yang et al. 2014). This in turn results in the release of several arbitrators of inflammation such as nitric oxide (NO), prostaglandin E_2 and pro-inflammatory cytokines, and this further activates the chemotactic reactions of other inflammatory cells, resulting in the synthesis of hydrolytic enzymes and cytotoxic molecules (Labow et al. 2001). The reaction of organisms towards this would be the migration of immune cells via the endothelial cells (Nathan 2002). Inflammation response results in the elimination of possible pathogens, thereby, returning the damaged tissue back to the condition of homeostasis (Lawrence and Gilroy 2007). Homeostasis is the tendency towards a relatively stable equilibrium between the interdependent elements and is maintained by physiological processes. The vital role being played by both the acute and the chronic inflammatory responses as a natural defense mechanism of the body's innate immune system for the maintenance of immune homeostasis (Barton 2008). However, if the inflammation is not controlled adequately, it can spread in the entire body and may result in several tissue damages including gastritis and other associated organs. Moreover, oxidative stress and inflammation are strongly correlated with each other (Ceriello and Motz 2004). In addition to this, inflammation results in the

aggravation of oxidative damage and reduces anti-oxidant capacity of cells by overproducing various inflammatory mediators through mast cells associated with the release of cytokines from macrophages as well as the production of neutrophils. Apart from this, inflammation is accompanied with the production of huge amounts of reactive oxygen species and nitrogen-derived free radicals, as a result of which tissues get severely destructed and DNA gets damaged. Increased amounts of reactive oxygen species can result into human disorders like cancer, cardiovascular disease and diabetes mellitus as well as neurodegenerative disorders such as Alzheimer's and Parkinson's disease (Surh and Packer 2005; Bennett and Brown 2003).

The enzymes having characteristic feature of getting induced are the main targets of the anti-inflammatory drugs because these enzymes cause the production of a large number of pro-inflammatory mediators like the enzymes from the arachidonic acid pathways (phosphor-lipase, lipoxygenase and cyclo-oxygenase) and hyaluronidase. The steroidal or the non-steroidal anti-inflammatory drugs are used in treating inflammation but such drugs usually have unexpected side effects and they are also not regarded as a good clinical choice for chronic inflammatory disorders and these drugs exhibit their action through the inhibition of these enzymes via different mechanisms (Khansari 2009). Another mode of action for the anti-inflammatory drugs is by inhibiting the generation of reactive oxygen species or through their scavenging (Vane and Botting 1998). It has been demonstrated in different studies that there exists a strong bond between the anti-inflammatory and the anti-oxidant properties (Werz and Steinhilber 2005; Mateo Anson et al. 2011). Yet, the consumption of anti-inflammatory drugs over a prolonged period of time is associated with a great amount of secondary effects, thereby, increasing the costs in healthcare. Therefore, it should be of great interest to search novel natural alternative sources of drugs for treating chronic inflammatory pathologies. A significant role in human health is being played by natural products with respect to preventing and treating inflammatory conditions (D'Almeida et al. 2013). One of the most important aspects of complementary medicines is herbal medication, and the process of inflammation has several mechanisms and number of treatment methods consequently. A large numbers of cytokines participate in the activation of enzyme (like phospholipase A2), mediator release, fluid extravasation and vasodilation and cell migration (Fig. 4.2) (Ghasemian et al. 2016).

4.2 Anti-inflammatory Effects of Plant Extracts

Anti-inflammatory activity is one of the most reported effects among the different biological activities of natural plant products that have been published till the present time. The extract obtained from winter season collected *Calamintha nepeta* exhibited anti-inflammatory activities as it caused 40.10% inhibition of COX-2 production (Pacifico et al. 2014). The shoot methanolic extract of the halophyte *Limonium densiflorum* exhibited best anti-inflammatory activity by inhibiting 80% release of nitric oxide at a concentration of 160 μg/mL in LPS-stimulated RAW

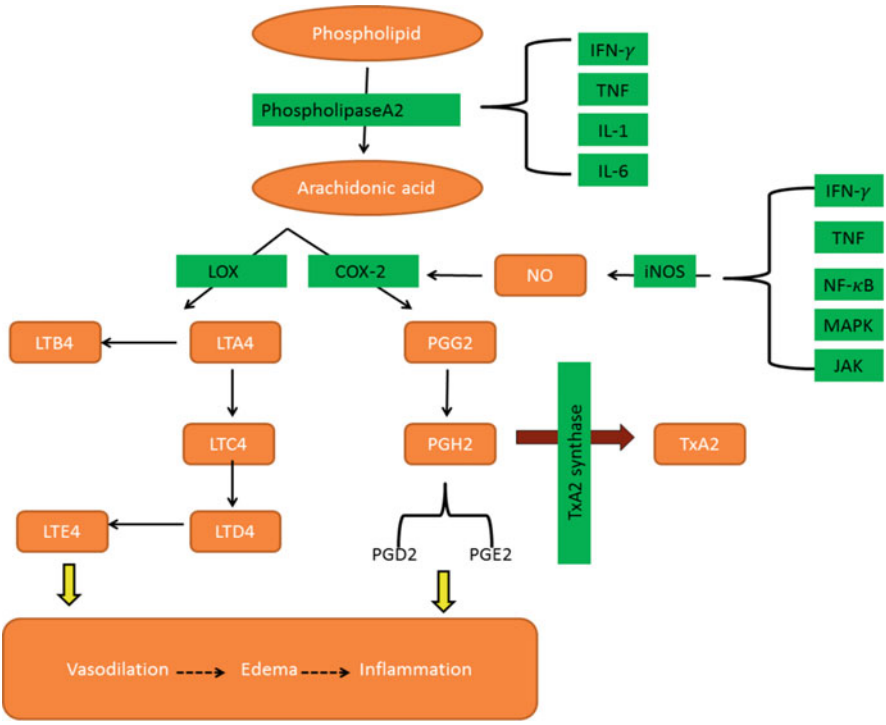


Fig. 4.2 Inflammation pathway. COX, cyclooxygenase; LOX, lipoxygenase; PG, prostaglandin; LT, leukotriene; TX, thromboxane; NO, nitric oxide; iNOS, inducible NO synthase; IFN, interferon; TNF, tumor necrosis factor; NF-κB, nuclear factor-κB; MAPK, mitogen activated protein kinase; JAK, Janus kinase; IL, interleukin (Adapted from Ghasemian et al. 2016)

264.7 cells (Medini et al. 2015). The aqueous methanolic leaf extract of strychnine tree (*Strychnos nuxvomica*) exhibited promising anti-inflammatory activity (Omayma and Abdel-Daim 2015). Determination of the molecular mechanism behind the prevention of HCl/EtOH-instigated gastric ulcers in mice due to the methanol extract of *Persicaria chinensis* against lipopolysaccharide-instigated PGE2 and nitric oxide in RAW264.7 macrophages revealed that it remarkably reduced the expression of lipopolysaccharide-instigated pro-inflammatory cytokines including interleukin-β, interlukin-6, and tumor necrosis factor-α. Also, the activation as well as phosphorylation of activator protein-1 and mitogen-activated protein kinase was decreased in both differentiated U937 cells as well as lipopolysaccharide-instigated RAW264.7 cells. Thus, these results were strongly indicative of methanolic extract of *P. chinensis* as a remedy that suppresses mitogen-activated protein kinase (MAPK)/activator protein (AP-1)-mediated inflammation processes (Hossen et al. 2015b). Across India, *Jasminum sambac* L. is cultivated and its roots and leaves are utilized traditionally to treat fever, pain and inflammation. It has been reported that its leaves exhibit remarkable anti-inflammatory activity. In the year 2015, Sengar et al. revealed that at a concentration of 400 mg/kg, the root extract of

J. sambac prepared in ethanol exhibited remarkable anti-inflammatory activity after 2nd, 3rd, 4th and 6th hours of treatment in carrageenan-instigated edema and a 33.58% inhibition in cotton pellet-instigated granuloma production was also found at the similar dosage amount. Moreover, this extract also remarkably ($p < 0.001$) produced inhibition in arthritis instigated by adjuvant (Sengar et al. 2015). *Phyllanthus acidus* is being utilized traditionally in the treatment of respiratory disorders, gastric trouble, hepatitis, bronchitis, rheumatism and asthma. In a study conducted by Hossen et al. (2015a), the methanolic extract of the aerial parts of *P. acidus* resulted in the suppression of nitric oxide and prostaglandin-E2 synthesis as well as caused prevention of morphological alterations associated with lipopolysaccharide-treated RAW 264.7 cells. Moreover, this extract resulted in the down-regulation of the expression of inducible nitric oxide synthase and cyclooxygenase-2 as well as caused reduction in the nuclear levels of NF-κβ. Among the flavonoids that were identified, quercetin and kaempferol were found to be partially active anti-inflammatory compounds in the methanolic extract of the aerial parts of *P. acidus*. Thus, it was concluded that the methanolic extract of the aerial parts of *P. acidus* exhibited anti-inflammatory effects in vivo as well as in vitro through the suppression of Syk, Src and their downstream transcription factor, NF-κβ (Hossen et al. 2015a). The anti-inflammatory activity of methanolic extracts from two different stages of *Dendropanax morbifera* (green and senescent leaves) revealed that they showed a strong suppression in the synthesis of LPS-instigated pro-inflammatory cytokines as well as mediators by suppressing the expression of inducible nitric oxide synthase and cycloxygenase-2 and also inhibited the ERK1/2 signaling pathway. Moreover, the analysis of phenolic compounds through high performance liquid chromatography (HPLC) revealed that the leaf extracts comprised of active phenolic compounds like myricetin, quercetin, rutin, chlorogenic acid, resveratrol, (+)-catechin and ferulic acid which were considered responsible for the anti-inflammatory properties (Hyun et al. 2015).

Inflammation and pain have been reported to be responsible for various pathological conditions. The extract prepared in methanol and ethyl acetate fraction of *Acacia hydaspica* exhibited anti-inflammatory effect in carrageenan-instigated paw edema in rats; 150 mg/kg of the dose was markedly efficient to a greater extent resulting in 91.92% suppression. Moreover, the methanolic extract and ethyl acetate fraction of *A. hydaspica* exhibited the highest suppression of edema at a dose of 150 mg/kg after 4 h on prostaglandin E2 (PGE2)-instigated edema in rats (Afsar et al. 2015). *Pistacia lentiscus* has been utilized in Algeria in treating burns, inflammation and gastrointestinal problems. Its leaf extract (100 g/mL) exhibited remarkable anti-inflammatory effect than acetylsalicylic acid (ASA) indicating that *P. lentiscus* extracts possessed anti-inflammatory property in line with its conventional utilization (Remila et al. 2015). The extracts of *Clausena anisata*, at a concentration of 6.25 μg/mL, caused 96% inhibitions in the synthesis of nitric oxide by RAW 264.7 macrophage cell lines in vitro (Adebayo et al. 2015). The extract of *Ocimum labiatum* showed potential to inhibit inflammation at a concentration of 25 μg/mL without any cytotoxic effect and caused remarkable ($p < 0.05$) inhibition in the synthesis of pro-inflammatory cytokines, interlukin-4, interlukin-2,

interlukin-17A and interlukin-6. (Kapewangolo et al. 2015). Crude extract obtained from the fruits of *Nitraria schoberi* exhibited potential to inhibit the inflammation of the order of 36.12%, 59.89%, and 88.33% at 100, 200 and 500 lg/mL, respectively (Sharifi-Rad et al. 2015). For mankind, roots as well as herbaceous parts of leguminous crops have not been utilized generally because these have been conventionally regarded as waste substances. Despites not regarded as consumable, such parts of leguminous crops have a complex chemical composition possessing remarkable biological potentials. Keeping in view such potentials, the herb extracts of *Phaseolus vulgaris* and *Cicer arietinum* were evaluated for anti-inflammatory potential and were found to be potent suppressors of TXS enzyme in cyclooxygenase pathway, making these extracts important sources of protective agents against inflammation, cardiovascular diseases and thrombosis. Therefore, these results were indicative of a strong capability of waste legume material as a potential source to isolate bioactive anti-inflammatory as well as anti-oxidant compounds to be utilized as therapeutic as well as dietary additives in the food as well as pharmaceutical industry (Sibul et al. 2016). The methanolic extract of the aerial parts of *Xanthium strumarium* exerted anti-inflammatory activity by suppressing the synthesis of nitric oxide as well as prostaglandin E2. Also, oral treatment with this extract improved HCl/EtOH-instigated gastric lesions. Hence, it was concluded that this extract exerted in vitro as well as in vivo anti-inflammatory potential through the inhibition of PDK1 kinase action, which in turn blocked the signal to its downstream transcription factor, NF-κβ (Hossen et al. 2016). In conventional system of medicine, *Saposhnikovia divaricata* is utilized for the treatment of inflammation, arthritis and pain. The potential of *S. divaricata* extract to inhibit inflammation was investigated in vitro in RAW 264.7 cells treated with lipo-polysaccharide. It was found that this extract exhibited anti-inflammatory activity through the production inhibition of prostaglandin-E2, tumor necrosis factor-α, nitric oxide and interleukin-6 in RAW 264.7 cells instigated with lipopolysaccharide (LPS). Moreover, this extract also resulted in the inhibition of the synthesis of pro-inflammatory cytokines as well as arbitrators (Chun et al. 2016). In the folk medicines, *Salvia fruticosa* is utilized on a large scale. The ethyl acetate extracts of both the roots and the aerial parts of *S. fruticosa* exhibited significant anti-inflammatory potential which was partly correlated with the radical scavenging capacities of their polyphenolic constituents (Boukhary et al. 2016).

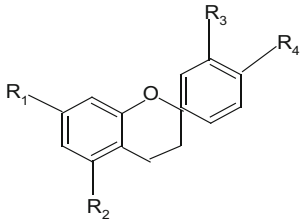
Cymbopogon citratus is among one of the known aromatic plants being used throughout world in the conventional system of medicine for curing inflammation associated conditions. The in vivo topical anti-inflammatory potential of *C. citratus* infusion (CcI) as well as *C. citratus* flavonoids fraction (CcF) and *C. citratus* tannins fraction (CcT) in the carrageenan-instigated rat paw edema model revealed that at a concentration of 4% and 1%, *C. citratus* infusion (CcI) exhibited an edema decrease of 43.18% and 29.55%, whereas, CcF + CcT decreased 59.09% edema separately (Costa et al. 2016). The extracts of *Lavandula dentata* and *L. stoechas* possess immunomodulatory potential because they in vitro down-regulated varying inflammatory arbitrators such as nitric oxide as well as cytokines. In addition to this, modulation of the expression of pro-inflammatory chemokines and cytokines was

also observed due to these extracts. It was concluded that the extracts of *L. dentata* and *L. stoechas* had impact to suppress inflammation and to inhibit inflammation in the region of intestine and other body parts, affirming their potent utilization as herbal remedies in the gastrointestinal ailments (Algieri et al. 2016).

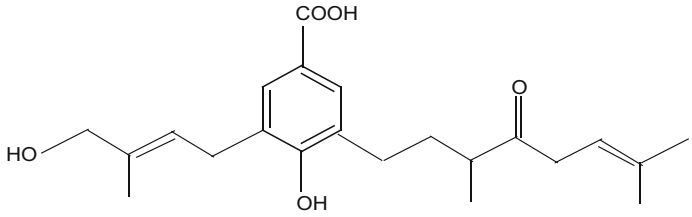
The species of *Stryphnodendron*, popularly named "barbatimao," have been utilized traditionally in Brazil as anti-inflammatory agents. The study conducted by Henriques et al. (2016) reported that the extracts of *Stryphnodendron obovatum*, *S. adstringens*, *Terminalia glabrescens* and *Campomanesia lineatifolia* inhibit tumor necrosis factor-α in a concentration dependent manner, thereby, revealing anti-inflammatory activity (Henriques et al. 2016). The anti-inflammatory activities of the bark ethanolic extract of *Mimosa tenuiflora* and solvent soluble fractions (hexane-H, DCM-D, EtOAc-E and BuOH-B) of the extract in vivo was indicative of the fact that the bark ethanolic extract exhibited anti-inflammatory potential through the reduction of neutrophil migration to the peritoneal cavity as well as in the plantar tissue which was determined via decreased myeloperoxidase activity, decreased IL-10 levels as well as expression of ICAM-1 in the peritoneal exudate and the mesentery. Moreover, the three soluble fractions (H, D, E) also showed good anti-inflammatory results (Cruz et al. 2016).

The anti-inflammatory activities of seeds, leaves and few Brazilian native fruits (*Eugenia myrcianthes, E. leitonii, E. brasiliensis* and *E. involucrata*) were determined in an in vivo model by utilizing the technique of carrageenan-instigated migration of neutrophil in the acute phase and it was observed that the seeds, pulp and leaves of these fruits decreased the influx of neutrophil by 40–64%. Therefore, these results were suggestive of the anti-inflammatory property of these fruits due to the modulation of neutrophil migration, retardation of chemokines, cytokines, and adhesion molecules. Hence, these fruits can be used in the production of food additives as well as functional foods (Infante et al. 2016). The hydroalcoholic extracts of *Frankenia triandra* prepared through maceration and soxhlet extraction exhibited a remarkable retardation of hyaluronidase as well as two enzymes of arachidonic acid pathway, that is, lipoxygenase and cyclooxygenase-2, thereby, exhibiting anti-inflammatory potential related to the anti-oxidant properties (Carro et al. 2016). The *Buddleja crispa* crude extract (50–200 mg/kg i.p.) as well as its hexane fraction inhibited carrageenan-instigated rat paw edema with a maximum retardation of 65% and 71%. Moreover, the anti-inflammatory capacity of its extract as well as the isolated pure compounds could be compared to that of diclofenac sodium (Bukhari et al. 2016). Analysis of the dried leaves of *Eriodictyon angustifolium*, a North American shrub, revealed eight active compounds that exhibited a profound potential to suppress inflammation (Fig. 4.3) (Walker et al. 2016).

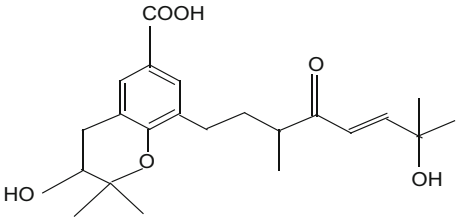
The leaf extract of *Anacardium occidentale* can be used to manage inflammation, and oleamide has been found to be one of the most bioactive component attributed for its anti-inflammatory potential (Awakan et al. 2018). It has been reported in a study that the extract of *Physalis angulata* calyces exhibited the highest in vivo anti-inflammatory potential in 12-*O*-tetradecanoyl-phorbol-13-acetate (TPA)-instigated mouse ear edema and also exhibited impact on the synthesis of pro-inflammatory



R_1=R_2=R_3=R_4=OH ; Eriodictyol
R_1=R_2=R_4= OH, R_3= H ; Naringenin
R_1=R_2=R_4= OH, R_3= OMe ; Homoeriodictyol
R_1=R_2=R_3= OH, R_4= OMe ; Hesperetin
R_1= OMe , R_2=R_3=R_4=OH ; Sterubin
R_1=R_2= OH , R_3= H, R_4= OMe ; Isosakuranetin



Erionic acid C



Erionic acid B

Fig. 4.3 Active anti-inflammatory compounds identified from *Eriodictyon angustifolium* (Walker et al. 2016)

mediators in vitro. Further, fractionation of this extract was carried and it was found that its dichloromethane fraction was the most potential fraction in vitro, suppressing the synthesis of prostaglandin E2, nitric oxide, tumor necrosis factor-α, monocyte chemotactic protein, interleukin (IL)-1b and IL-6. Moreover, this fraction significantly inhibited penetration inside tissue (Rivera et al. 2018). The in vitro potential of different concentrations of aqueous root extract of *Syzygium caryophyllatum* to inhibit inflammation through heat-instigated egg albumin denaturation bio assay process has also been established (Heendeniya et al. 2018). Among the crucial health issues are pain and inflammation that have been usually cured through conventional treatments chiefly through the help of medicinal crops. Anti-inflammatory effect of 80% methanolic leaf extract of *Leonotis ocymifolia* in rodent models decreased 75.88% paw edema after 6 h of instigation with carrageenan. Also, it was observed that all the studied doses of extract remarkably retarded the synthesis of granuloma

as well as inflammatory exudates (Alemu et al. 2018). The ethanolic extract and alkaloids total fraction obtained from the aerial parts of *Cissampelos sympodialis* possess the anti-inflammatory activity as they exhibited reduced amounts of tumor necrosis factor-α and interlukin-1β and elevated the amounts of interlukin-10 and glutathione–glutathione (de Sales et al. 2018).

Similarly, the ethanolic extract of *Ajuga laxmannii* exhibited the anti-inflammatory effect through the reduction of polymorpho-nuclear leukocytes, total leukocytes, oxidative stress and phagocytosis. The studies in comparison to diclofenac, 50 mg/mL of *A. laxmannii* extract exhibited better anti-oxidative stress and anti-inflammatory effects. Therefore, such findings were strongly suggestive of *A. laxmannii* as a precious source of bioactive compounds that can be further valued as anti-inflammatory agents in preparing various herbal drugs (Toiu et al. 2018). The polyphenol-abundant extract from the leaves of *Syzygium aqueum* exhibited promising anti-inflammatory activities in vitro by inhibiting lipoxygenase, cyclooxygenase-1 and cyclooxygenase-2 having a higher cyclooxygenase-2-selectivity as compared to diclofenac and indomethacin plus decreased the extent of erythrocytes lysis when incubated in hypotonic buffer. Moreover, the extract also remarkably decreased the amount of leukocyte having same activities to diclofenac in the rats that were treated with carrageenan. The observed anti-inflammatory activities were attributed to some affinity of the identified polyphenolics from the extract for the active pockets of cyclooxygenase-1, cyclooxygenase-2 and 5-lipoxygenase (Sobeh et al. 2018). Anti-inflammatory activity of the hydro-methanol leaves' extract of *Allophylus africanus* on laboratory rats has shown that doses of 250 and 1000 mg/kg resulted in remarkable anti-inflammatory activity at the 3rd, 4th and 5th hours having a dose-dependent effect at the 4th and 5th hours. Moreover, significant decrease of paw edema in the rats was also observed (Ibrahim et al. 2018). The plants *Rhus tripartitum* and *Periploca laevigata* possess anti-inflammatory activity as they reduced the release of nitric oxide as well as reactive oxygen species in J774A.1 macrophages, *P. laevigata* possessed more anti-inflammatory effect (Ncib et al. 2018). The ethanolic extract of *Ziziphus jujuba* possessed remarkable ability to cause inhibition of carrageenan-instigated paw edema in the female Wistar rats ($p \leq 0.05$) and it also had an effect on the paw volume as well as the thickness of both left and right paws than the negative control group (Mesaik et al. 2018). The flowers of *Opuntia ficus* resulted in significant inhibition of inflammation in carrageenan-instigated rat paw edema model which was affirmed through the histological and the hematological determination and this was associated with the decreased amount of malondialdehyde and elevation in the action of superoxide dismutase, reduced glutathione and catalase. Therefore, these results are indicative of the use of flowers of *Opuntia ficus* as a natural source to treat inflammatory disorders (Ammar et al. 2018). The photoprotective activity of hydroalcoholic extract of red propolis in a murine model when given topically and the protective mechanisms have been associated with the anti-inflammatory and anti-oxidant properties of compounds present (Batista et al. 2018). The high anti-inflammatory potential in the extracts of *Peganum harmala* and *Marrubium alysson* prepared in the methanol has also been observed (Edziri et al. 2018). The reverse

phase-HPLC was indicative of coumarin as the compound present in abundance in the extract of *Hertia cheirifolia* L. (53.80% made in methanol). When this extract was administered at 100 mg/kg, the maximum acute anti-inflammatory potential was observed in rats, thereby promoting the conventional utilization of this plant in treating diseases related to inflammation (Majouli et al. 2018).

Anti-inflammatory effects of the extracts of *Feretia apodanthera* against the right hind paw's edema of albino rats, thereby, could play the role of an efficient antioxidant (Owolabi et al. 2018). A total of 200 and 400 mg/kg doses of *Brucea antidysenterica* possess a significant anti-inflammatory effect (Tessema et al. 2018). The ethyl acetate fraction of the leaves of *Tetraclinis articulata* exhibited anti-inflammatory activity with an EC_{50} value of129.67 μg/mL (Rached et al. 2018). The bio-available fraction from the species of *Origanum* significantly inhibited the secretion of TNF-α, IL-1β and IL-6 in the human THP-1 macrophages model (Villalva et al. 2018). Studies on the anti-inflammatory activity of *Scutellaria barbata* revealed that the ethanol fraction was comprised mainly of flavonoids and phenolics, whereas, the ethyl acetate fraction was comprised mainly of chlorophylls as well as carotenoids. Moreover, both the extracts were capable of remarkably inhibiting synthesis of lipopolysaccharide-instigated prostaglandin E_2, nitric oxide, IL-1 β and IL-6. Both the extracts were found to exhibit a dose-dependent anti-inflammatory potential on RAW 264.7 cells. Therefore, this study was suggestive of using *S. barbata* extract as an anti-inflammatory medium for the feasible biomedical utilization in the coming years (Liu et al. 2018).

The anti-inflammatory assay conducted on the oil/extracts of *Thymus vulgaris* and extracts of *Chlorella vulgaris* depicted a potential synergistic impact as they reduced the LPS-instigated increase of nuclear factor-κ, tumor necrosis factor-α, inducible nitric oxide synthase, cyclooxygenase-2, nitric oxide as well as oxidative stress. Hence, it was concluded that the Greek *T. vulgaris* extracts possessed anti-inflammatory activities that can be potentiated upon mixing with the extracts of *Chlorella vulgaris* (Habashy et al. 2018). The anti-inflammatory potential of *Bupleurum marginatum* methanolic and dichloromethane extracts carried in the in vitro and in vivo experiments revealed that the release of prostaglandin-E2 was decreased by 41.33% and 52.85% at a concentration of 25 μg/mL, whereas, 5-lipoxygenase was retarded with IC_{50} values of 45.28 and 25.92 μg/mL. Moreover, it was also observed that the methanolic and dichloromethane extracts decreased the diameter of the carrageenan-instigated rat paws' edema by 50% and 70%, respectively (Ashour et al. 2018). Some typical flavanones or extracts obtained from the buds of *Populus* x *burliness* and *P. nigral* reduced the liberation of IL-1β as well as IL-6 in HGF-1 cells along with down-regulation of their mRNA (Pobocka-Olech et al. 2018). The extract of *Piper cubeba* prepared in methanol exhibits anti-inflammatory activity through action on Src/Syk in the nuclear factor-κB pathway (Qomaladewi et al. 2019). Likewise, another study revealed that the 80% extract obtained from the leaves of *Calpurnia aurea* prepared in methanol possess anti-inflammatory potential (Ayal et al. 2019). *Anthocleista vogelii* ethyl acetate fraction possesses the anti-inflammatory activity at 100 mg/kg and the results shows that it inhibited 37.8%, 62.5% and 69.7% of edema instigated through egg-albumin at the

2nd, 4th and 6th hours which was attributed to the non-cytotoxic terpenoids present in this fraction (Eze et al. 2019). The anti-inflammatory effect of the extract of *Portulaca oleracea* is due to the suppression of lung inflammation as it reduced interlukin-6, interleukin-β, prostaglandin-E2, tumor necrosis factor-α and transforming growth factor-β, whereas, it elevated the amounts of interlukin-10. Thereby, it was concluded that the extract of *Portulaca oleracea* exhibited anti-inflammatory potential towards lipopolysaccharide-instigated rat acute lung injury (Rahimi et al. 2019). Elicitation of *Levisticum officinale* leaves with 0.1% yeast extract and 10 μM jasmonic acid elevated the anti-inflammatory activity (Złotek et al. 2019). *Kalanchoe brasiliensis* and *K. pinnata* possess confined potential to inhibit inflammation and the formulations comprising aqueous extract of both these plants decreased ear as well as paw edema which was established through decreased activity of interlukin-1β, myeloperoxidase, interlukin-1β, and tumor necrosis factor-α amounts and elevated interlukin-10 amounts (de Araújo et al. 2019).

4.3 Anti-inflammatory Activity of Essential Oils

Essential oils (EOs) possess important volatile compounds with diverse bioactivities including anti-microbial potential and used in drugs, food, and cosmetics (Chouhan et al. 2017). EOs are complex mixtures of substances being biologically active that are classified as natural products possessing pharmacological activity that can be of therapeutic use to manage human diseases (Derwich et al. 2010). The EOs extracted from medicinal and aromatic plant species are among the natural compounds that are gaining particular attention as they possess radical scavenging activities (de Sousa Barros et al. 2015). The direct incorporation of aromatic plants' EOs to foodstuffs exhibit an anti-oxidant and anti-microbial effect (Costa et al. 2015). The oral administration of *Citrus limon* EOs at a dose of 50, 100 and 150 mg/kg remarkably decreased the number of writhes and the highest doses decreased the number of paw licks, thereby, exhibiting anti-inflammatory activity (Ficarra et al. 2015). The coriander oil exhibits anti-inflammatory potential in the ultraviolet (UV) erythema test in vivo (Reuter et al. 2008). The anti-inflammatory activity from EOs of *Origanum ehrenbergii*, *O. syriacum* and *O. ehrenbergii* was studied in lipopolysaccharide-instigated inflammation in RAW264.7 cells and a significant decrease in NO production was observed (Loizzo et al. 2009). The anti-inflammatory effect of *Cyperus rotundus* EOs in carrageenan-instigated rats revealed significant ($p < 0.01$) dose dependent reduction from 2nd hour after carrageenan injection in paw edema rats. This essential oil also resulted in the inhibition of inflammatory pain ($p < 0.01$) at a dose of 500 mg/kg, whereas, the pain due to inflammation was significantly ($p < 0.05$) blocked at lower doses (Biradar et al. 2010). The anti-inflammatory potential of cumin volatile oil in carrageenan-instigated rat paw edema indicated that the volatile oil of cumin exhibited dose-dependent inhibition of the rat paw edema at a dose of 0.1 mL/kg, i.p. than the control group. Moreover, the anti-inflammatory activity was found to be comparable with that of the standard drug, diclofenac

sodium (Shivakumar et al. 2010). Further in the same year, Chouhan et al. (2011) showed the dose-dependent reduction of carrageenan-instigated rat paw edema by the *Crotalaria juncea* seed oil. Also, remarkable ($p < 0.001$) anti-inflammatory effect was exhibited by *C. juncea* seed oil at a dose of 200 mg/kg during the late inflammation phase comparable to that of diclofenac sodium (Chouhan et al. 2011). The anti-inflammatory effect of extra virgin olive oil from *Olea europaea* in carrageenan-induced paw edema in rats was found similar to that of treatment with dexamethasone (Fezai et al. 2013). As revealed by real-time PCR tests, cumin EOs caused remarkable inhibition of the mRNA expressions of inducible nitric oxide synthase, cyclooxygenase-2, interleukin-1, and IL-6 in lipopolysaccharide-instigated RAW 264.7 cells. Further, Western blotting analysis indicated that cumin EOs caused blockage of LPS-induced transcriptional activation of nuclear factor kappa β (NF-κβ) as well as inhibition of the phosphorylation of extracellular signal-regulated kinase (ERK) and c-Jun N-terminal kinase (JNK). Hence, it was concluded that cumin EOs exhibited anti-inflammatory effects in LPS-stimulated RAW264.7 cells by inhibiting NF-κβ and mitogen-activated protein kinases ERK and JNK signaling (Wei et al. 2015). Garlic oil exhibited anti-inflammatory potential by inhibition of the assembly–disassembly processes of the cytoskeleton (Hussein et al. 2017). *Citrus limetta* EOs comprised of limonene as well as monoterpene hydrocarbon being the chief constituent. When macrophages were pre-treated with the EOs of *C. limetta*, inhibition in the synthesis of pro-inflammatory cytokines such as interlukin-6, tumor necrosis factor-α, interlukin-1β in the lipopolysaccharide-instigated inflammation and inhibition in the synthesis of reactive oxygen species in H_2O_2-instigated oxidative stress was also observed. On the other hand, in vivo study revealed that when the volatile oil was applied topically, it had the ability in reducing 12-*O*-tetradecanoylphorbol-13-acetate-instigated ear weight, ear thickness, synthesis of pro-inflammatory cytokines, lipid peroxidation as well as improved the histological damage in the ear tissue (Maurya et al. 2017). The two components cinnamaldehyde and linalool distilled and extracted from the fresh leaves of *Cinnamomum osmophloeum* have shown remarkable anti-inflammatory potential and affirm the potent utilization of this essential oil as an anti-inflammatory natural product as well as gave proof that linalool and cinnamaldehyde were the two potential compounds for prophylactic utilization in inflammations associated health issues which were assigned to the hyper-activated TLR4 and/or NLRP3 signaling pathways (Lee et al. 2017). The EOs from half ripe *Citrus myrtifolia* decreased the synthesis of nitric oxide as well as the expression of inflammatory genes, cyclooxygenase-2 and inducive nitric oxide synthase, cytokines, including interleukin-1 and interleukin-6, and chemokine monocyte chemotactic protein-1 by lipopolysaccharide-instigated RAW 264.7 macrophages. Moreover, the chief components that were identified in the EOs of *Citrus myrtifolia* were linalool, limonene, linalyl acetate and γ-terpinene (Plastina et al. 2018). IC_{50} value of 0.97 μg/mL has been established regarding the in vitro anti-inflammatory activity of the volatile oil of *Siegesbeckia pubescens*, thereby reducing the capability of lipopolysaccharide-instigated RAW264.7 macrophages to liberate nitric oxide. On the other hand, the EOs of *Siegesbeckia orientalis* having an IC_{50} value of 14.99 μg/

mL was able to inhibit the lipopolysaccharide-instigated liberation of cytokine interlukin-6 (Gao et al. 2018). The EOs of *Rosmarinus officinalis* also possess anti-inflammatory activity through the inhibition of NF-κβ transcription and suppression of arachidonic acid cascade (Borges et al. 2018). Likewise, *Pistacia lentiscus* fatty oil resulted in a remarkable reduction of interlukin-6, nitric oxide and tumor necrosis factor-α levels in the ex-plant culture supernatants. Moreover, the *P. lentiscus* fatty oil also decreased the expression of inducible nitric oxide synthase expression in the gastric mucosa (Boutemine et al. 2018). *Pimpinella anisum* (aniseed) EO non-toxic doses remarkably reduced the expression amounts of interlukin-1 as well as interlukin-8 along with the elevated secretion of Muc5ac lipopolysaccharide-treated tracheal epithelial cell lines (HBEpC and HTEpC). Moreover, EOs also exhibited a remarkable anti-inflammatory impact on both HBEpC and HTEpC cells together along with the increased secretion of mucus (Iannarelli et al. 2018).

The chemical composition of *Croton campestris* EOs comprised of 1,8-cineol (16.98%), caryophyllene (15.91%) and germacrene-D (14.51%) among the chief components. It was observed that 1,8-cineol and germacrene-D exhibited anti-inflammatory potential in the abdominal contortions, paw edema induced by carrageenan, histamine, dextran and arachidonic acid models, the formalin test, peritonitis test and vascular permeability. The β-caryophyllene, on the other hand, showed no remarkable impact on the granuloma assay (de Morais Oliveria-Tintino et al. 2018). It was observed that EOs of *Thymus camphoratus* exhibited more pharmacological potential than the essential oil of *T. carnosus* than the volatile oil of *T. carnosus* exhibiting inhibition ion potential towards nitric oxide synthesis at smaller concentrations of 0.16 μL/mL and a concomitant inhibition of the expression of two important pro-inflammatory proteins, cycloxygenase-2 and inducible nitric oxide synthase at a concentration of 0.32 μL/mL. As the quenching of nitric oxide activity was not observed, it was concluded that the anti-inflammatory potential of the two EOs occurred upstream of inducible nitric oxide synthase expression, probably by inhibiting relevant pro-inflammatory signal transduction pathways (Zuzarte et al. 2018). The first study on the leaf essential oil of *Psidium guineense* demonstrated that it possessed anti-inflammatory property when orally administered in mice, thereby, remarkably inhibited the carrageenan-instigated mice paw edema in pleurisy model (do Nascimento et al. 2018). Likewise, the first report on the anti-inflammatory potential of pure coconut oil was due to the suppression in the inflammatory markers (Varma et al. 2019). The anti-inflammatory potential of volatile oil extracted from the leaves of *Curcuma caesia* has been observed ((IC_{50}value 182.5 μg/mL)) (Borah et al. 2019). The volatile oil of *Santolina corsica* possesses potential to inhibit and to suppress inflammation on the bronchial tract of hospitalized patients reported with respiratory ailments of hospitalized patients recovered with respiratory ailments (Foddai et al. 2019). It has also been established that EOs of *Rosmarinus officinalis* possess potential to inhibit inflammation against macrophages, thereby, making this oil as a potential anti-inflammatory medium (Lorenzo-Leal et al. 2019). The EOs of *Stachys subnuda* possess medium in vitro anti-inflammatory potential having an IC_{50} value of 0.419 mg/mL (Sen et al. 2019).

4.4 Anti-inflammatory Effects of Isoflavones

The most absorbable and bioavailable flavonoids are isoflavones that have been originally considered as an anti-inflammatory agent as genistein causes down-regulation of cytokine-instigated events of signal transduction in immune system cells (Verdrengh et al. 2003; Yu et al. 2016). After this, large number of investigations frequently showed that isoflavones possess anti-inflammatory properties. The isoflavone genistein exhibited potential to inhibit inflammation in mouse models that affected monocytes, granulocytes and lymphocytes (Verdrengh et al. 2003). The diets comprising of isoflavone help in the prevention of inflammation-related instigation of metallothionein in the intestine and prevent inducing manganese superoxide dismutase in the mice liver injected with endotoxin lipopolysaccharide. It also inhibits the reaction of intestine to inflammation by altering the activity of pro-inflammatory cytokine interleukin-6 (Paradkar et al. 2004). The isoflavone powders (derived from processed soybean cake, a byproduct of the soybean oil industry) and genistein standard efficiently caused inhibition of lipopolysaccharide-instigated inflammation, reduction in the amount of leukocyte in mouse blood, as well as decreased the synthesis of interlukin-6, interlukin-1, prostaglandin-E2 and nitric oxide in the supernatant of peritoneal cells' exudates and the fluid of peritoneal exudates (Kao et al. 2007). Tests in human on the consumption of a soy nut diet for 8 weeks (340 mg isoflavones/100 g soy nut) revealed decreased markers of inflammation like interlukin-18 and C-reactive protein and elevated titers of nitric oxide levels in the plasma of postmenopausal women with metabolic syndrome (Azadbakht et al. 2007). Such in vivo observations have depicted that various isoflavones exhibit anti-inflammatory potentials consistently in multiple animal models, whereas, in vitro studies in various cultured cells have also revealed the anti-inflammatory capability of isoflavones. The pre-treatment with genistein decreased the lipopolysaccharide-instigated amount of cycloxygenase-2-protein and nitric oxide in the supernatant of primary cultures of human chondrocytes, with no effect on the amount of cycloxygenase-1 protein (Hooshmand et al. 2007). Genistein mediated inhibition of cycloxygenase-2 than cycloxygenase-1 is superior because suppression of COX-2 can decrease the synthesis of pro-inflammatory particles (Hooshmand et al. 2007). The methanol fraction of soybean comprising of isoflavones exhibits potential to inhibit inflammation in the experimental replica of ear edema instigated by croton oil (Carrara et al. 2008). Puerarin, a distinctive isoflavone, has been able to save the brain of rats from ischemic damage after middle cerebral artery blockage. This effect was attributed to the anti-inflammatory potential of puerarin through the expression inhibition of cycloxygenase-2 in microglia and astrocyte (Lim et al. 2013). It has been reported in a study that isoflavone daidzein stops tumor necrosis factor-α-instigated elevation in the expression as well as activity of pro-inflammatory chemokine Cxcl2, along with a marked inhibition of tumor necrosis factor-α-instigated protein poly-adenosine diphosphate-ribosylation in murine lung epithelial cells (Li et al. 2014). The THP-1 monocyte cells of humans have been reported to be suppressed by daidzein because of the LPS-instigated amounts of interlukin-6, interlukin-12, and tumor necrosis

factor-α (Tanaka et al. 2014). It has been found that the isoflavone-abundant soy foods too decrease the amount of serum C-reactive protein in the end-stage patients of renal failure as well as the amount of interferon in healthy volunteers (Ferguson et al. 2014).

Extensive epidemiological studies, together with in vivo and in vitro experiments in the current times, revealed that isoflavones give benefits to those patients having cardiovascular diseases, osteoporosis and cancer (Messina 2014). Pre-treatment with genistein decreased nitric oxide and prostaglandin-E2, and inhibited the synthesis of D-galactosamine-instigated pro-inflammatory cytokines, including tumor necrosis factor-α and interlukin-1β in the male Wistar rats (Ganai et al. 2015). Genistein stops homocysteine-instigated death of vascular endothelial cell, morphological alterations of cells and reactive oxygen species' synthesis, thus, indicating that genistein blocked injury of endothelial cell due to inflammation (Han et al. 2015). The anti-inflammatory characteristics of isoflavones have been addressed in cell cultures, animals and clinical trials with the underlying mechanisms being elucidated in many studies. Although, it is still unclear about the mechanisms of isoflavones actions, various possibilities have been well unrevealed (Yu et al. 2016).

4.5 Anti-inflammatory Effects of Polyphenols

The phenolics compounds having an aromatic ring possess one hydroxyl group while "poly-phenols" possess one or more aromatic rings having more than one hydroxyl group. The chemical structures of polyphenols are chiefly associated with their anti-oxidant, anti-inflammatory activities and other biological functions (Zhang and Tsao 2016). The dietary intake of foods enriched with polyphenols like fruits and vegetables reduces the chances of degenerative diseases due to oxidative stress and inflammation (Chuang et al. 2014). Inflammation as well as oxidative stress can result in the pathogenesis of chronic diseases and metabolic disorders. The anti-inflammatory potentials and the activity related to anti-oxidation stress due to phenolics can essentially affect similar biomarkers (Chuang et al. 2014). Supplementations of kaempferol or quercetin caused alteration of inflammation or insulin resistance in adipocytes by activating peroxisome proliferator-activated receptor-g, which is a nuclear receptor that regulates degradation of fatty acid and metabolism of glucose (Fang et al. 2008). *p*-coumaric acid is reported to cause inhibition of inflammasome-mediated secretion of interlukin-1β as well as the activation of caspase-1 in the macrophage cells of ex vivo inflamed mouse (Hori et al. 2013).

The flavonoids such as procyanidin β2 and apigenin have also been reported to be capable of inhibiting inflammasome activation and interlukin-1β secretion in the lipopolysaccharide-instigated human macrophages (Martinez-Micaelo et al. 2015). The stilbene phenolic compound named resveratrol present in red grapes also caused inhibition of NLRP3 activation-instigated autophagy for the preservation of mitochondrial function in both in vitro as well as in vivo studies. Moreover, resveratrol also improved hepatic inflammation in high-fat diet-instigated obesity mouse model

(Chang et al. 2015). The flavonoids and their metabolites are among the varieties of phenolic compounds that have been observed to agonistically control PPAR-g activation via ligand interaction (Wang et al. 2014). The phenolic compounds obtained from dietary sources like plant foods, herbs and spices can trigger PPAR-γ to reveal protagonist consequences on the transcription factors of inflammation, resulting in the repression of inflammation and inhibitory consequence on the metabolic diseases. A nicotinamide adenosine dinucleotide-dependent protein deacetylase sirtuin (SIRT)-1 control epigenetic gene silencing in response to stress causes the regulation of the NF-kβ signaling transductions as well as elevates insulin sensitivity (Anastasiou and Krek 2006). As PPAR-g coactivator (PGC-1a) and SIRT-1 interacts, activation of PPAR-g with flavonoids can thus effect SIRT-1-controlled signaling transductions comprising the transcriptional factor NF-κβ (Davis et al. 2009). Resveratrol has an agonistic action on SIRT-1 for the protection of cells from inflammatory damages (Chen et al. 2009). Since, the dietary polyphenols have less absorption rate, less amounts of such compounds having physiological relevance can still alter the expression of several inflammatory bio-markers through different signaling pathways. In order to produce effects, therapeutical drugs target these biomarkers, therefore, the capability of dietary phenolics on the same pro-inflammatory cytokines as well as other signaling molecules can have significant positive effect in preventing chronic non-communicable diseases due to oxidative stress. The protagonistic role of dietary phenolics is the topmost feature involved behind their anti-inflammatory mechanisms (Zhang and Tsao 2016).

4.6 Role of Fermentation in Increasing Anti-inflammatory Properties of Herbs

The easiest as well as safe traditional method for the enrichment of useful bioactive compounds is fermentation, as this method upgrades biological properties of herbs, vegetables and plants. This process is associated with the decomposition and/or biotransformation of complex substrates into the compatible constituents, thus, either alters the product' properties or the amount of some bioactive components (Chouhan et al. 2019). Accumulating evidences are indicative of enhanced anti-inflammatory potentials of herbs that have undergone through the process of fermentation. A rate-limiting enzyme, namely cycloxygenase-2, exhibits regulatory effect in the production of various inflammatory mediators that are active in biological systems, like prostaglandin-E2, which is also activated in various carcinomas, thereby, indicating its important part in inflammation as well as tumor genesis (Chouhan et al. 2019). The protein, namely cycloxygenase-2, and synthesis of prostaglandin-E2 in RAW 264.7 cells are triggered due to lipopolysaccharide (Mathers et al. 2006). The changed profile of secondary metabolites and changes in their mechanisms that affect biological activity having therapeutic enhancement are positively associated with fermentation because this process increases the amount of bioactive components like anti-oxidants, and also the anti-inflammatory activity of

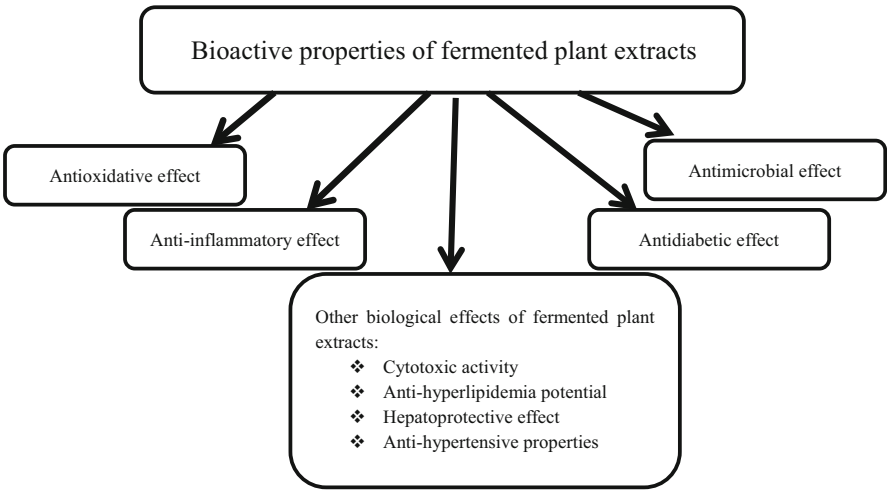


Fig. 4.4 Bioactive properties of fermented plant extracts

several compounds gets ameliorated (Chouhan et al. 2019). Inhibition of the translocation of NF-κβ p65 occurred because of the fermented OY-reduced degradation of Iκβα and through the phosphorylation of extracellular kinases that are signal regulated, and p38 and c-Jun more strongly as compared to the unfermented OY. Thus, it was concluded from these findings that fermentation increased the potential of the anti-inflammatory effect of OY by obstructing NF-κβ and MAPK pathway in the macrophage cells (Seo et al. 2005). Obstruction of expression of cycloxygenase-2 due to BST204 is not dependent on NF-κβ and mTOR/p70 S6 kinase pathway and some other pathways of undetermined nature had been reported to be the mediators for this (Seo et al. 2005). Fermentation resulted in significant increase in the obstructive impact of Oyaksungisan because of fermentation against the expression or synthesis of numerous vital pro-inflammatory mediators, namely cycloxygenase-2, tumor necrosis factor-α, inducible nitric oxide synthase, nitric oxide, prostaglandin-E2 and interlukin-6 in RAW 264.7 cells (Oh et al. 2012). Fermented preparation of *Rhizoma atractylodis* macrocephalae remarkably reduced the potential of NF-κβ upon co-treatment of lipopolysaccharide-instigated RAW 264.7 cells (Bose and Kim 2013). The activity of NF-κβα gets inhibited through the fermented *Artemesia princeps* in the lipopolysaccharide-instigated peritoneal macrophages (Joh et al. 2010). The co-treatment of lipopolysaccharide-instigated RAW 264.7 cells with the leaf extract of guava that has undergone fermentation could significantly suppress the transcriptional activity of NF-κβ in a concentration-dependent manner (Choi et al. 2008). Therefore, it was suggested that fermented leaf extract of guava could obstruct the activation of NF-κβ through suppressing Iκβα deterioration stimulated due to lipopolysaccharide (Choi et al. 2008). A schematic presentation of bioactive properties of fermented plant extracts is shown in Fig. 4.4.

4.7 Conclusion

The information presented in this chapter indicates that many extracts, essential oils and compounds derived from natural products exhibit potent anti-inflammatory properties. In the recent studies, it has been established that these extracts, essential oils and compounds derived from natural products possess significant modulatory effect on cellular biomarkers that are related to oxidative stress and inflammation, which results in reducing the risk of many chronic diseases. By reviewing the potent role of plant extracts, essential oils and compounds derived from natural products along with their mechanisms on oxidative stress and inflammation-related biomarkers, it is hoped that future efforts in this respect can focus on increasing the bioaccessibility, bioavailability from processing and formulation of plant-based functional foods, and ultimately this will develop functional foods or nutraceuticals that will decrease health risk of chronic diseases because of their modulatory effects. Although production of drugs from the plant-based anti-inflammatory compounds may prove a difficult task, but plant extracts, essential oils and pure compounds of natural products may still open new areas for therapeutic interventions.

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