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Review Article

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Anti-Inflammatory Constituents of Plants: A Review

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ABSTRACT

Inflammation is seen as a protective response of tissues to harmful stimuli and inflammatory disorders are synonymous to man's existence owing to lifestyle changes, environmental hazards and genealogical influences. In many folk medicines, crude drugs are the first line treatment in these conditions. The aim of this review was to survey some anti-inflammatory constituents from plant sources, their mechanism(s) of actions and their structural types using some published academic articles. The survey revealed many chemical moieties as anti-inflammatory agents and also implicated alkaloid, flavonoid, terpenoid, steroid, coumarin and anthraquinone as the major chemical classes of compounds with various mechanisms of actions that are associated with anti-inflammatory processes. This study lends credence to the fact that there are many chemical entities in plants that could serve as anti-inflammatory agents and also concludes the involvement of many chemical classes of compounds as anti-inflammatory in activity.

Keywords: Anti-inflammatory; Constituents; Plants

INTRODUCTION

The term inflammation is part of the complex biological response of body to harmful stimuli such as pathogens, damaged cells or irritants [1]. It is a protective mechanism aimed at eliminating the initial cause of cell injury, clearing out necrotic cells and damaged tissues from the original insult hence initiating repair and thus could be said to be a protective response involving immune cells, blood vessels and molecular mediators. The classical signs of inflammation include; heat which is as a result of the stimulus; pain which is due to the release of chemicals e.g. bradykinin and histamine that stimulate nerve endings; oedema due to the accumulation of fluid;

redness as a result of increased blood flow to the area and loss of function due to the insensitivity of the nerve endings. Inflammation may be acute or chronic depending on the duration of the stimuli. Acute inflammation is the initial response of the body to harmful stimuli and usually lasts from the onset to about 3 months. The process of acute inflammation is initiated by resident immune cells present in the tissue involved in the damage such as macrophages, dendritic cells, histiocytes, kupffer cells and mast cells. This process begins to cease once the mediators are degraded as most of them have short lifespan and also when the stimulus is removed [1].

Chronic inflammation is a condition that arises from persistent acute inflammation due to non-degradable pathogens, stimuli, persistent foreign bodies and immune system that last up to six (6) months and above. It is characterized by mononuclear cells (monocytes, macrophages, lymphocytes, plasma cells) and fibroblasts. It has a delayed onset with cytokines (IFN-Y), growth factors, reactive oxygen species (ROS), hydrolytic enzymes being the primary mediators with resultant outcome of tissue destruction, fibrosis and necrosis. Inflammatory processes are involved in many diseases ranging from rheumatoid arthritis, asthma, chronic inflammatory bowel diseases, type-2 diabetes, neurogenerative disorders and cancer hence the need for more probes into moieties that could help ameliorate this menance [1,2].

MANAGEMENT OF INFLAMMATION

NSAIDs

The non-steroidal anti-inflammatory drugs (NSAIDs) can be taken to alleviate the pain and oedema caused by inflammation. The NSIADs are a very diverse group of drugs and they all inhibit group of enzyme called “cyclo-oxygenase” (COX). COX exists in many tissues and inhibition of this enzyme reduces the amount of chemicals known as “prostaglandins” in these sites. Prostaglandins are lipid autacoids derived from arachidonic acid by the actions of the COX enzymes and play many roles such as vasodilatation, maintenance of local homeostasis in the body and the production of inflammation. The COX enzymes are of varieties and also play prominent physiological roles. For instance, COX-1 is known to protect gastric epithelial cells and also prevent kidney from damage while COX-2 are involved in ovulation and labour. COX-1 is more involved in the normal functioning of organs like the stomach, while COX-2 is more involved when inflammation starts to occur. Most of the NSAIDs inhibit both COX-1 and COX-2 thereby causing adverse effects experienced when the non-selective NSAIDs are used for a long time. There are few NSAIDs that selectively inhibit COX-2 and these “COX-2 selective inhibitors” reduce the risks of some of the side effects associated with NSAIDs therapy [2].

Analgesic Drugs

Owing to the fact that inflammation at most times are associated with pains, the use of pain relievers is also necessary. The most effective analgesics by far are the opioid analgesics. The opioids include all drugs that interact with opioid receptors in the nervous system. These receptors are the sites of action for the endorphins, compounds that already exist in the body and are chemically related to the opioids that are prescribed for pain. Opiods consist of several classes but they have their limitations that restrict their use to in patient management [2].

Corticosteroids

Two types of corticosteroids (glucocorticoids and mineralocorticoids) are known. The glucocorticoids are mostly used as anti-inflammatory agents. Glucocorticoids are potent anti-inflammatory agents and regardless of the inflammation's cause, they inhibit the synthesis of lipocortin-1 (also known as annexin-1). Lipocortin-1 inhibits phospholipase A2 hence leading to reduced release of arachidonic acid thereby blocking the production of prostaglandins and leukotriene. Glucocorticoids may also be used in low doses in adrenal insufficiency. In much higher doses, oral or inhaled glucocorticoids are used to suppress various allergic, inflammatory and autoimmune disorders and inhaled glucocorticoids are the second-line consideration for asthma [3,4].

Inflammation Diets

Several foods have been shown to be helpful in the management of inflammation. Some of these items of diets are olive oil, tomatoes, nuts (walnuts and almonds), leafy greens (spinach), fatty fish (salmon and mackerel) and fruits. While these dietary solutions do not alone hold the key to controlling inflammation, they can help prime the immune system to react in a measured way [5].

Anti-inflammatory Constituents of Plants

Plants from inception have been the first source of drugs and remedies for the treatment and management of human ailments irrespective of cultural belief hence the involvement of plants in different traditional systems of medicines such that in most developing countries, herbal medicine is still a choice in addition to the use of orthodox drugs and other procedures [6]. Many reports from researches have implicated many molecules as anti-inflammatory agents. Some of the constituents of plants established as anti-inflammatory agents are as presented in Table 1.

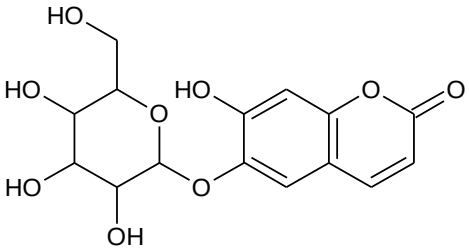
Table 1. Constituents of plants established as anti-inflammatory agents

S/N	Medicinal Plant	Family	Anti-inflammatory Constituent	Proposed Mechanism of Action	References
1	Aesculus hippocastanum	Sapindaceae	Esculin 1 (Coumarin)	Inhibition of	[7,8]

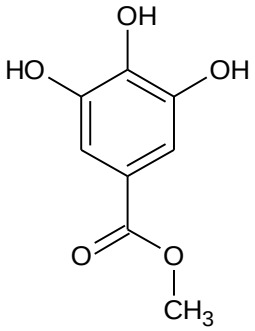
	(Horse chestnut)			prostaglandin synthesis	
2	Alchornea cordifolia (Christmas bush)	Euphorbiaceae	Methyl gallate 2 (Triterpenoid, Phenolic)	Inhibition of COX-1	[9]
3	Alchornea floribunda (Christmas bush)	Euphorbiaceae	Eugenol 3, cardinal 4, linalool 5, caryophylene, (E)-a-bergamotene (Terpenoids)	Inhibition of COX-1 and COX-2	[10]
4	Alchornea cordifolia (Christmas bush)	Euphorbiaceae	4-methyl-1-isopropyl-(R) -3- cyclohexene -1- ol(19) (Terpenoids)	Inhibition of COX-1 and COX-2	[10]
5	Allium cepa (Red Onions)	Amaryllidaceae	Quercetin 6 (Phenolic) (Anthraqinone)	Inhibition of NFkB, MARK and STAT-1	[11,12]
6	Aloe vera	Aspodelaceae	Aloe-emodin 7	Inhibition of inducible nitric acid and prostaglandins	[13]
7	Artemisia scoporia(Virgate wormwood, Capillary wormwood, Red stem wormwood)	Asteraceae	Scoparene 8 (Coumarin)	Inhibition of prostaglandin synthesis	[14]
8	Boswellia serrate (Boswella, Boswellin)	Bursecaceae	Boswellic acid 9 (Triterpenoid)	Inhibition of 5-lipoxygenase, hence leukotriene biosynthesis	[15]
9	Cannabis sativa (Hemp, marijuana)	Cannabaceae	Canniprene 10 (Dihydro-stilbene)		[16]
10	Capsicum annum (Pepper)	Solanaceae	Capsaicin 11 (Alkaloid)	Inhibition of TRPVI, a non selectivecation channel	[17]
11	Camellia sinensis (Tea plant)	Theaceae	Epigallocatechin-3-gallate 12 (Phenolic)	Inhibition of NFkB, MARK and COX-2	[18,19]
12	Colchicum autumnale (Autumn crocus, Meadow saffron)	Colchicaceae	Colchicine 13 (Alkaloid)	Inhibition of NFkB, COX-2 and AP-1	[20,21]
13	Curcuma longa (Tumeric)	Zingiberaceae	Curcumin 14 (Phenolic)	Inhibition of NFkB, COX, MARK and LOX	[22-24]
14	Cammiphora mukul (Guggul, Gum Guggul)	Burseraceae	Guggulsterone 15 (Steroid)	Inhibition of prostaglandin synthesis	[25]
15	Daucus carotasyn.sativus (wild carrot, bird's nest, bishop's lace)	Apiaceae	Umbelliferone 16 (Coumarin)	Inhibition of prostaglandin synthesis	[8,26]
16	Evodia rutaecarpa (Evodia)	Rutaceae	Evodiamine 17, Rutaecarpine 18 (Alkaloids)	Inhibition of COX-2 and prostaglandin (PGE-2)	[27]
17	Eupatorium cannabinum (Hemp-agrimony, Holy rope)	Asteraceae	9-0-angeloyl-8,10-dihydrothymol 19 , 9-(3-methylbutanoyl)-8,10-dehydrothymol 20 , 2-hydroxy-2,6-dimethylbenzofuran-3 (2H)–on and 1-(2hydroxy-4-methylpheny)propan-1, 2	Inhibition of COX-1 and COX-2	[28]

			dione 21 (Terpenoids)		
18	Fraxinus rhychophylla (Ash)	Oleaceae	Fraxetin 22 (Coumarin)	Inhibition of prostaglandin synthesis	[7,8]
19	Glycyrrhiza glabra (Licorice, Liquorice)	Fabaceae	Glycyrrhetinic acid (Pentacyclic triterpenoid)	Inhibition of histamine, serotonin and bradykinin	[29,30]
20	Handroanthus impetiginosus (Brazilian taheeda)	Bignoniaceae	Anthraquinone-2-carboxylic acid (Anthraqinone)	Inhibition of inducible nitric acid and prostaglandins	[31]
21	Handroanthus impetiginosus (Brazilian taheeda)	Bignoniaceae	Lapachol 23 (Phenolic)	Inhhibition of 5-LOX	[32]
22	Kaempferia galangal (Galanga, Resurrection lily)	Zingiberaceae	Ethyl-methoxycinnamate 24	Inhibition of COX-1	[33]
23	Malus pumila	Rosaceae	Quercetin (Phenolic)	Inhibition of NFkB, MARK and STAT-1	[12,34]
23	Magnolia fargesii syn. Officinalis (Houpumagnolia or Magnolia-bark)	Magnoliaceae	Scopoletin 25 (Coumarin)	Inhibition of prostaglandin synthesis	[7,8,29]
24	Ocimum gratissimum (Clove basil)	Lamiaceae	Eugenol 3 ,linalool 5 , D-fenchone, I-terpene-4-ol, thymol, a-caryophylene (Terpenoids)	Inhibition of COX-1 and COX-2	[35]
25	Oenothera biennis (Evening Primrose)	Onagraceae	α–λινολενιχ αχιδ 26 (Φαττψ Αχιδ)	Inhibition of 5-lipoxygenase, LOX and 15-HEPE	[36]
26	Phyllanthus amarus (Stonebreaker, gale of the wind, seed-under-leaf)	Eurphorbiaceae	Nirtetralin 27		[37]
27	Rhaphiostylis beninensis	Icacinaceae	N,N-di(4-methoxybenzyl) thiourea 28	Inhibition of COX-1 and COX-2	[38]
28	Rubia tinctorum (Madder, dye's madder)	Rubiaceae	Purpurin 29 (Anthraqinone)	Inhibition of inducible nitricacid and prostaglandins	[39,40]
29	Solanum xanthocarpum (Wild eggplant)	Solanaceae	Solasodine (Steroidal glycoalkaloid)	Inhibition of COX-1, COX-2 and TNF-alpha.	[41]
30	Smilax officinalis (Red chinese root	Smilaceceae	Sarsasepogenin	Inhibition of prostaglandin synthesis, COX-1 and COX-2	[42]
31	Trigonella foenum-graecum (Sicklefruit)	Fabaceae	Diosgenin 30 (Steroid)	Inhibition of COX-1, COX-2 and TNF-alpha.	[43]
32	Vitis vinifera (Raspberries, Mulberries)	Vitaceae	Resveratrol 31 (Stilbene derivative)		[44]
33	Withania sominifera (Indian ginseng)	Solanaceae	Withanolide (Steroidal lactone)	Inhibition of prostaglandin synthesis, COX-1 and COX -2	[45,46]
34	Withania somnifera (Indian ginseng)	Solanaceae	β–χαρψοπηψλλενε	Inhibition of prostaglandin synthesis, COX-1	[47,48]

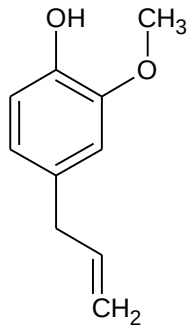
				and COX -2	
35	Zanthoxylum myriacanthum var. pubescens (Hairy mock orange)	Rutaceae	Decarine 32 (Alkaloid)	Inhibition of TNFα and IL-1B	[11]



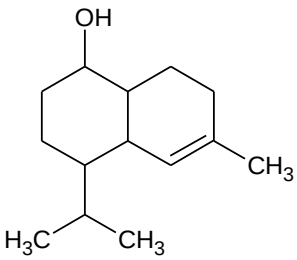
Esculin (**1**)



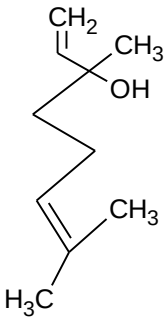
Methyl gallate (**2**)



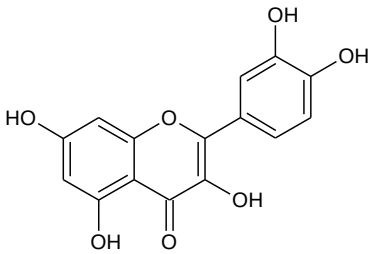
Eugenol (**3**)



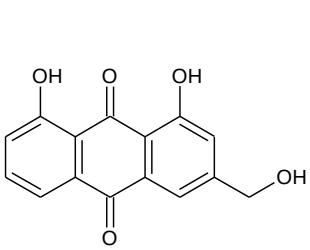
Cardinol (**4**)



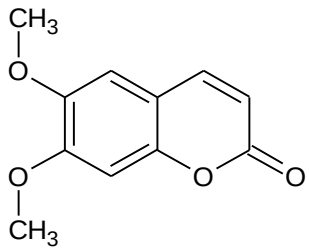
Linalool (**5**)



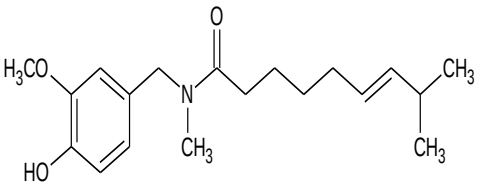
Quercetin (**6**)



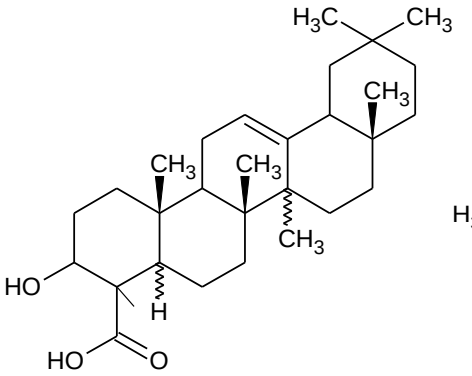
Aloe-emodin (**7**)



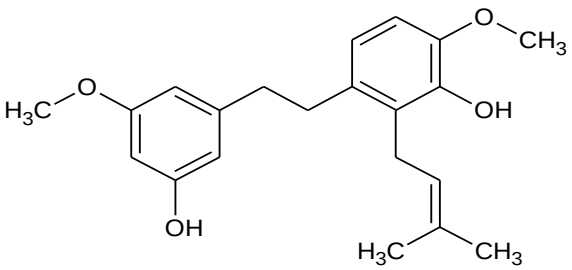
Scoparone (**8**)



Capsaicin (**11**)

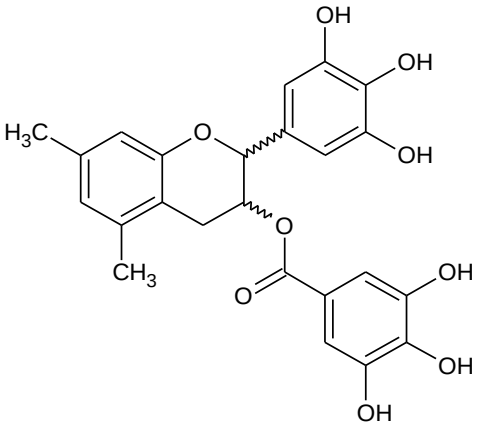


Boswellic acid (**9**)

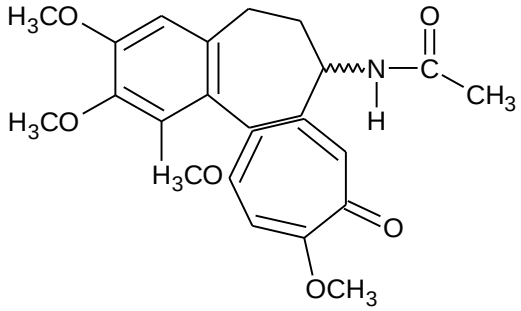


Canniprene (**10**)

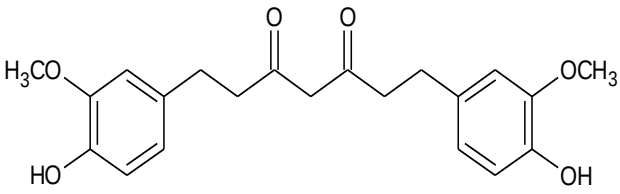
Representative structures of plant anti-inflammatory compounds 1



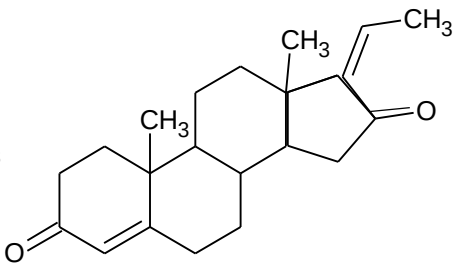
Epigallocatechin-3-gallate (**12**)



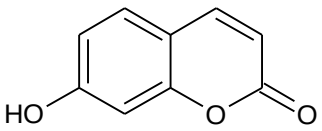
Colchicine (**13**)



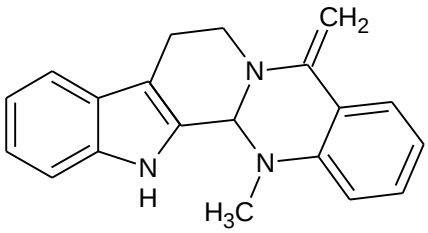
Curcumin (**14**)



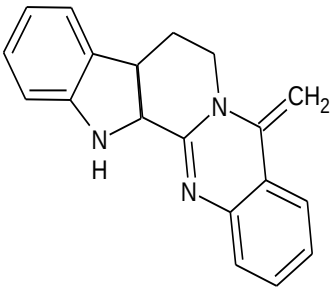
Guggulsterone (**15**)



Umbelliferone (**16**)

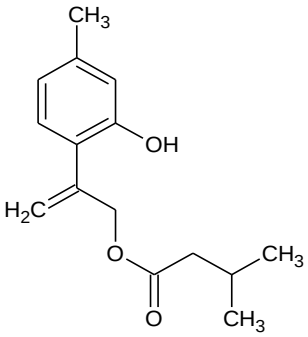


Evodiamine (**17**)

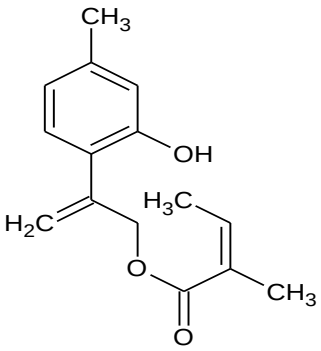


Rutaecarpine (**18**)

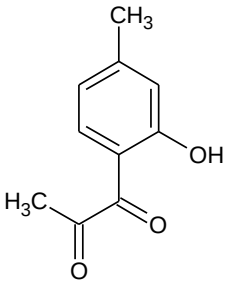
Representative structures of plant anti-inflammatory compounds 2



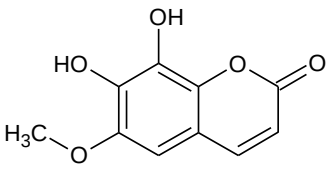
9-(3-methylbutanoyl)-8,10-dehydrothymol **(20)**



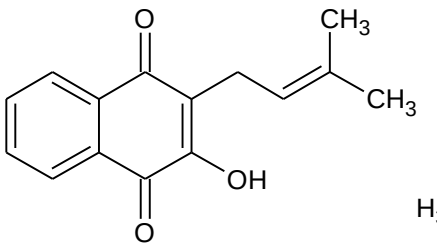
9-O-angeloyl-8,10-dihydrothymol **(19)**



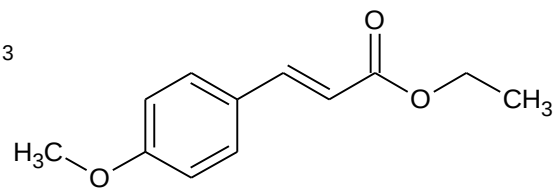
1-(2-hydroxy-4-methylphenyl) propan-,1,2-dione**(21)**



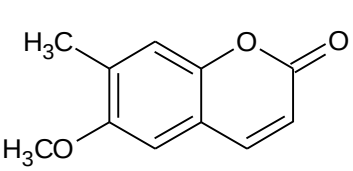
Fraxetin (**22**)

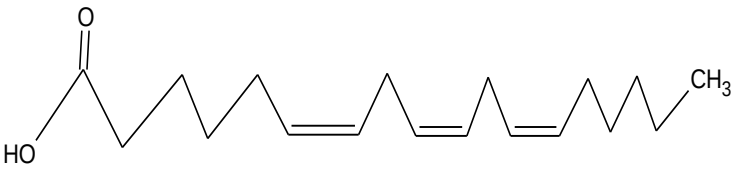


Lapachol (**23**)



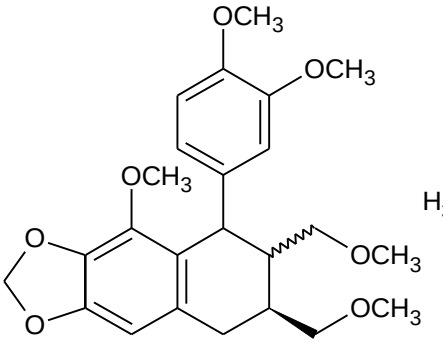
Ethyl -p-methoxycinnamate **(24)**

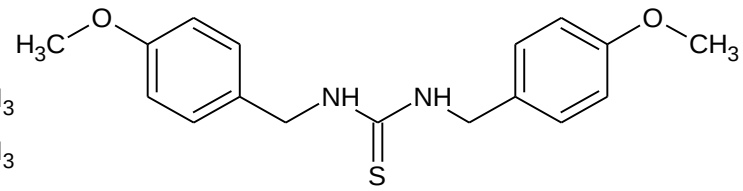




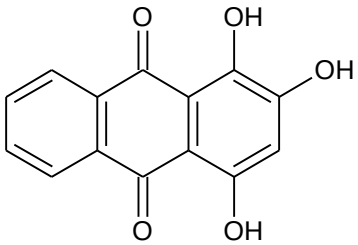
Scopoletin (**25**) Linoleic acid (**26**)

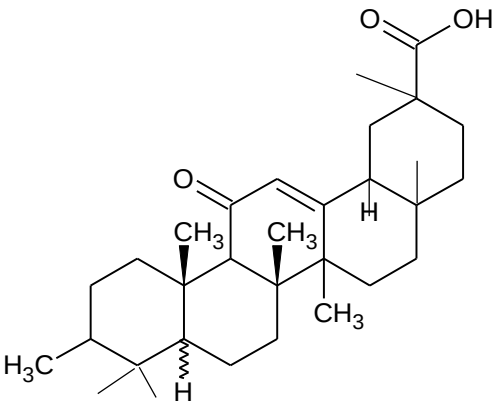
Representative structures of plant anti-inflammatory compounds 3



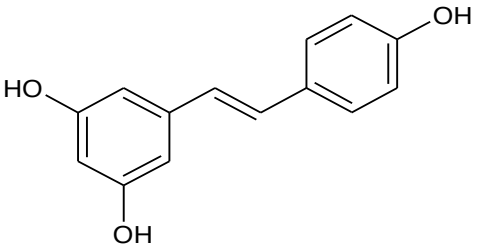


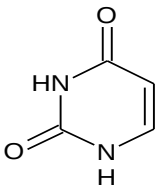
Nirtetralin (**27**) N,N-di(4-methoxybenzyl) thiourea **(28)**





1,2,4-trihydroxyanthraquinone (Purpurin) **(29)** Diosgenin **(30)**





Resveratrol (**31**) Decarine (**32**)

Representative structures of plant anti-inflammatory compounds 4

CONCLUSION

It is common knowledge that plants are the primary reservoirs of many moieties used as drugs in our today's world and the number of studies showcasing new drug molecules from plant sources in the area of inflammation management are enormous and is still in the increase hence underscoring the importance of plants in drug discovery. In essence only very few of these compounds found their way to clinical practice for the management of disorders associated with inflammation. Even though there are many academic articles describing these new compounds with their mechanisms of action(s), it is noteworthy to say that these data are based on *in vitro* models without corresponding *in vivo* modulation to truly mimic the human physiological hence the need for more clinical trials [7,22]. This review has shown that many compounds of diverse chemical varieties such as alkaloids, phenolics, terpenoids, steroids, coumarins, anthraquinones, stilbene derivatives are identified as anti-inflammatory agents through efforts of scientific researches. Since inflammatory processes are synonymous to man owing to the fact that man cannot isolate himself from these conditions due to poverty, lifestyle changes, genealogical affiliations among other factors, it becomes worthwhile for more researches to be carried out in this area to mitigate the effects of inflammation on the human race. More so, clinical trials should be encouraged on these compounds with the aim of making the potent ones add to the list of the available drugs used in the management of inflammation and its disorders.

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