Chapter 4

Terpenes from Natural Products with Potential Anti-Inflammatory Activity

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Additional information is available at the end of the chapter

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Abstract

The development and progression of many diseases is related with an inflammatory process, which could affect different organs or tissues. Currently, many drugs are used to treat inflammation. However, some of these compounds induce severe side effects. For this reason, the search of new therapeutic options for the treatment of inflammation is very desirable. Medicinal plants have been an interesting source for obtaining new active compounds, including several terpenes and terpenoids with anti-inflammatory activity. This book chapter includes 62 sesquiterpenes, 34 diterpenes, and 22 triterpenes with anti-inflammatory activity. The anti-inflammatory effect was evaluated using *in vitro*, *in vivo*, and both models. These terpenes were obtained from 44 plant species belonging to 25 botanical families. Eight of theses species belong to the Asteraceae family and four to Lamiaceae family, respectively, and the other species belong to 13 different botanical families, one sesquiterpene was obtained from a sponge and two diterpenes were isolated from corals.

Keywords: Terpenes, terpenoids, anti-inflammatory activity, natural, products

1. Inflammation

Inflammation is a response of vascularized tissues to infections and tissue damage, and contributes to the beginning and progression of diseases such as Alzheimer, type 2

diabetes, obesity, stroke, and cancer [1, 2]. The symptomatology of inflammation is characterized by pain, redness, swelling, heat, and loss of function. Depending on the time of duration, inflammation might be categorized into acute and chronic. Acute inflammation is considered as a protective response and occurs within minutes, hours, or few days after exposure to infections and/or tissue damage. Acute inflammation is characterized by the exudation of fluid (edema), elevated blood flow, and migration of neutrophils [3]. Chronic inflammation occurs when the initial response fails to repair tissue damaged or when a noxious stimulus is persistent, and is characterized with more tissue destruction, fibrosis, long presence of lymphocytes [4]. Macrophages, dendritic cells, and mast cells initiate the inflammatory process secreting pro-inflammatory cytokines such as interleukin 6 (IL-6) and interleukin 8 (IL-8), tumor necrosis factor-α (TNF-α), and inducing the production of reactive oxygen species (ROS), which play an important role in the modulation of inflammation [5]. The long-term use of current drugs for the treatment of inflammation, including nonsteroidal anti-inflammatory drugs (NSAIDs), the disease-modifying anti-rheumatic drugs (DMARDs), and steroids display several undesirable side effects such as gastric ulcers, nephrotoxicity, and hepatotoxicity, among others [6]. The search of new anti-inflammatory agents with less side effects is highly desirable. Furthermore, the efficient treatment of inflammation may be an interesting and effective way to prevent chronic diseases like cancer.

2. Terpenes

Natural products are a good source of anti-inflammatory compounds [7]. Terpenes, containing a C5 isoprene unit, are the large group of natural compounds found mostly in higher plants, but also in lower invertebrates. There are approximately more than 50,000 terpenes that have been isolated from different plant species. Terpenes, composed of isoprene units (C_5H_8), play a variety of vital roles in plant species, including growth and development and defense against herbivores and environmental stress [8]. Terpenes possess a great variety of biological activities as antimicrobial, against cancer, malaria, and anti-inflammatory effects in acute and chronic inflammatory conditions like chronic obstructive pulmonary disease and osteoarthritis [9, 10].

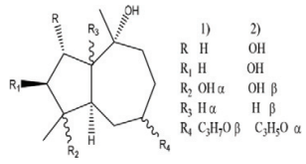
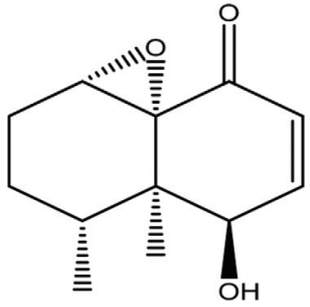
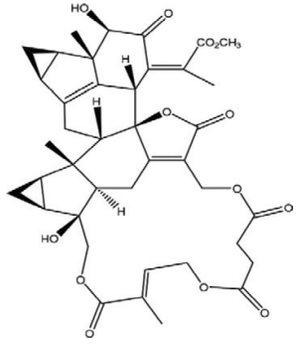
Cyperus rotundus, a perennial plant, has several pharmacological activities, including antibacterial [11], antimutagenic [12], and anti-inflammatory [13]. Isocyperol, a sesquiterpene isolated from the rhizomes of *C. rotundus*, inhibited the production of NO and PGE2, decreased the levels pro-inflammatory interleukins (IL-1β and IL-6) and the monocyte chemotactic protein-1 (MCP-1), and suppressed the gene expression of iNOS and COX-2 in RAW-264

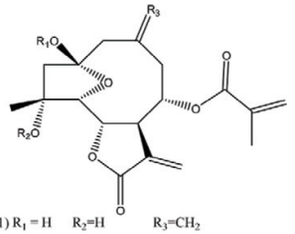
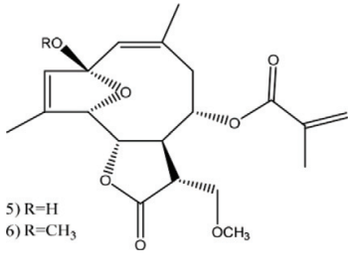
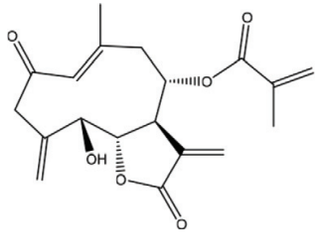
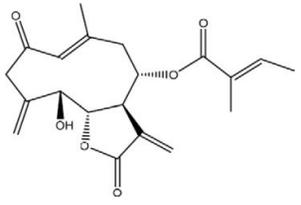
murine macrophages stimulated with lipopolysaccharide (LPS). In addition, isocyperol reduced the serum levels of NO, PGE2, and IL-6 in LPS-induced septic shock in mice, via suppression of the NF-κB and STAT3 signaling pathways [14]. *Dodonaea viscosa* induces gastroprotective [15], antibacterial [16], analgesic, and anti-inflammatory activities [17, 18]. Hawtriwaic acid, an ent-clerodane diterpene, was isolated from *D. viscosa* and showed anti-inflammatory activity on the murine ear edema induced with 12-O-tetradecanoylphorbol-13-acetate (TPA) by one or multiple applications. In both models, the compound diminished the edema [19]. Hawtriwaic acid at doses of 5, 10, and 20 mg/kg decreased knee inflammation in a murine model of monoarthritis induced with kaolin/carrageenan, by the reduction of serum levels of the pro-inflammatory interleukins Il-1β, IL-6, and TNF-α, and the increase in the serum levels of the anti-inflammatory interleukin IL-10 [20]. Ursolic acid, a pentacyclic triterpene found in many plant species, was identified for the first time in 1920 in the epicuticular waxes of apples. Ursolic acid exerts cytotoxic effects in various cancer cells by the inhibition of the STAT3 signaling pathway [21] and the induction of apoptosis [22]. Ursolic acid has protective effects on lung, kidney, liver, and brain, exerts anabolic effects on skeletal muscle [23], and induces antinociceptive activity in abdominal constriction test induced by acetic acid and the formalin test in mice [24]. Ursolic acid decreased the paw edema induced with carrageenan in rats [25], decreased the ear edema induced with Croton oil in mice [26], reduced the levels of iNOS, COX-2, IL-1β, IL-6, and TNF-α, and increased the level of IL-10 in macrophages stimulated with LPS [27].

The sesquiterpenes, vernomelitensin and onopordopicrin, isolated from *Onopordum illyricum* and the triterpene, Sootepin F, obtained from *Gardenia sootepensis,* decreased each NF-κB activity with IC_{50} values of 3.6, 8.6, and 20.3 μM, respectively [28, 29].

The pro-inflammatory enzymes: (1) inducible the nitric oxide synthase (iNOS), which is involved in the nitric oxide (NO) production, and the cyclooxygenase-2 (COX-2) involved in the prostaglandin production, are estimated in LPS-induced macrophages to evaluate the *in vitro* anti-inflammatory activity. IL-1 and TNF-α stimulate the production of NO. The inhibitory concentration 50 (IC_{50}) for these two pro-inflammatory enzymes has only been reported in some studies. The sesquiterpenes hydroxycostunolide (IC_{50} = 0.68 μM), costunolide (IC_{50} 0.3 μM), and artemorin (IC_{50} = 0.16 μM), obtained from *Inula montana*, showed similar or higher potency in the inhibition of NO, compared to that reported for the positive control dexamethasone (IC_{50} = 0.45–4.33 μM) [30]. Further studies are recommended to be performed with theses sesquiterpenes. Toxicological studies to guarantee their safety in long-term studies are also necessary. The *in vivo* studies evaluate swelling, redness, and pain mainly in rodents.

In the table is show the structure of 62 sesquiterpenes, 34 diterpenes, and 22 triterpenes with anti-inflammatory activity, isolated from 44 plant species, 1 sponge, and 2 corals.

Scientific name	Terpene	Structure	Anti-inflammatory assay	Results	Ref.
Sesquiterpenes					
Datura metel L.	**1)** 1β,5α,7β-Guaiane-4β,10α, 11-triol **2)** 1α,5 α,7 α −11- Guaiene-2 α,3β,4α,10α,13-pentaol		LPS-stimulated BV2 microglia cells.	The compounds **1** and **2**, tested at a concentration of 80 μM, each, inhibited the NO production by 37.5 and 46.0%, respectively.	[31]
Nardostachys chinensis Batal.	Nardosinanone N		LPS-stimulated RAW 246.7 macrophages.	The compound tested at 30 μM inhibited the protein expression of iNOS and COX-2.	[32]
Chloranthus henryi Hemsl.	Shizukaol B		LPS-stimulated BV2 microglia cells.	The compound (12.5–50 μM) suppressed in concentration-dependent manner the protein expression of iNOS and COX_2, and decreased the production of NO, TNF-α, and IL-1β.	[33]

Scientific name	Terpene	Structure	Anti-inflammatory assay	Results	Ref.
Elephantopus mollis Kunth.	**1)** 8-*O*-Methacryloyl-elephanpane **2)** 2,4-bis-*O*-Methyl-8-*O*-methacryloyl-elephanpane **3)** 4-*O*-Ethyl-8-*O*-methacryloyl-elephanpane **4)** 2,5-Epoxy-2β-hydroxy-4α-methoxy-8α-(2-methyl-propenoyloxy)-10(14),11(13)-germacratrien-12,6α-olide		LPS-stimulated RAW 264.7 macrophages.	The compounds inhibited the NO production with the following IC_{50} values (μM): **1** (2.09), **2** (2.18), **3** (4.06), **4** (4.82), **5** (14.34), **6** (59.97), **7** (0.57), **8** (2.17), **9** (2.02), **10** (1.95), **11** (11.25), **12** (1.09) **13** (1.21), **14** (6.95), and the positive control indomethacin (127.88).	[34]
	5) 2-*O*-Demethyl-tomenphantopin C **6)** Tomenphantopin C				
	7) Molephantin A				
	8) Molephantin B				

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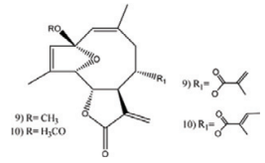
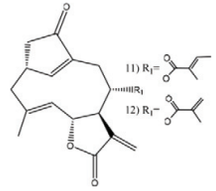
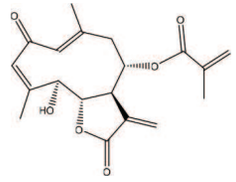
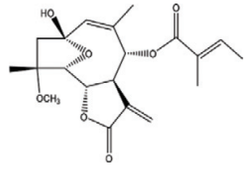
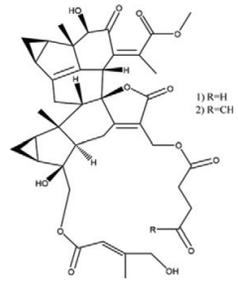
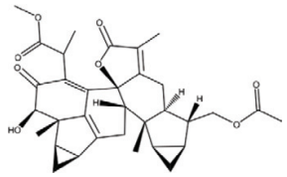
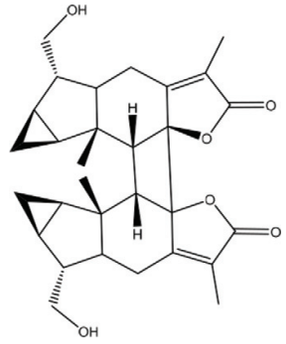
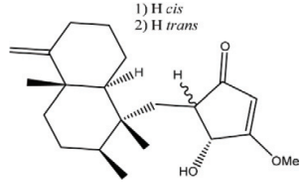
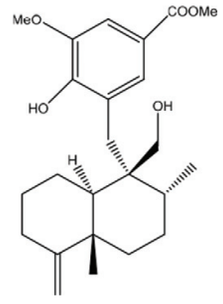
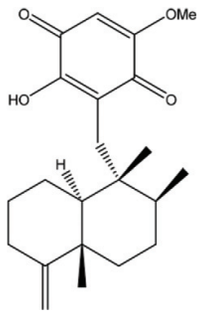
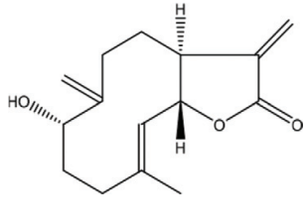
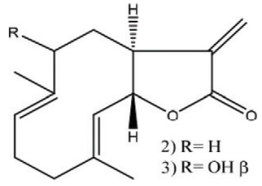
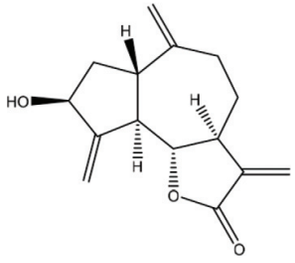
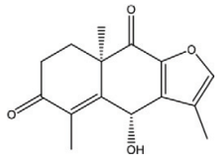
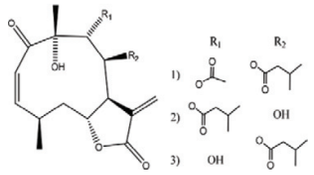
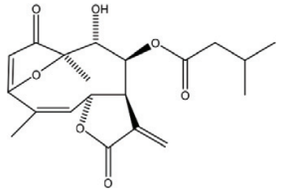
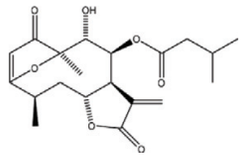
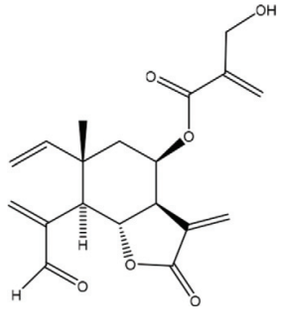
Scientific name	Terpene	Structure	Anti-inflammatory assay	Results	Ref.
	9) 2β-Methoxy-2-de-ethoxy-phantomolin **10)** 2β-Methoxy-2-deethoxy-8-*O*-deacyl-phantomolin-8-*O*-tiglinate				
	11) Scabertopin **12)** Isodeoxyelephantopi				
	13) Molephantin				
	14) 2, 5-Epoxy- 2β-hydroxy-4α-methoxy-8α-[(E)-2-methylbut-2-enoyloxy] -4(15), 10(14), 11(13)-germacratrien-12,6α-olide				
Chloranthus holostegius (Hand-Mazz) S. J. Pei & Shan.	**1)** Chololactone E **2)** Chololactone F		LPS-stimulated RAW 264.7 macrophages.	All compounds reduced NO production with IC_{50} (μM) values: **1** (8.5), **2** (6.9), **3** (3.5), **4** (4.4), and positive control dexamethasone (0.45).	[35]

Scientific name	Terpene	Structure	Anti-inflammatory assay	Results	Ref.
	3) Chololactone G				
	4) Chololactone H				
Smenospongia cerebriformis Duchassaing & Michelotti.	**1)** Smenohaimien A **2)** Smenohaimien B		LPS-stimulated BV2 microglial cells.	The compounds inhibited NO production **1** (IC_{50} 30.13 μM), **2** (IC_{50} 28.33 μM), **3** (IC_{50} 24.37 μM), **4** (IC_{50} 24.44 μM), and positive control l-NMMA (22.1 μM).	[36]
	3) Smenohaimien E				

Scientific name	Terpene	Structure	Anti-inflammatory assay	Results	Ref.
	4) Ilimaquinone				
Inula montana L.	**1)** Artemorin		LPS-stimulated RAW 264.7 macrophages.	The compounds inhibited the NO production with the following IC_{50} values (μM): **1** (0.16), **2** (0.3), **3** (0.68), and the positive control dexamethasone (4.33).	[30]
	2) Costunolide **3)** 9β-Hydroxycostunolide				
Ainsliaea yunnanensis Franch.	Zaluzanin C		LPS-stimulated RAW 264.7 macrophages.	The compound (IC_{50} 6.54 μM) reduced the NO production with similar potency, compared to the positive control amino guanidine (IC_{50} 7.30 μM).	[37]

Scientific name	Terpene	Structure	Anti-inflammatory assay	Results	Ref.
Chloranthus japonicus Siebold.	Chlorajaponol B		LPS-stimulated RAW 264.7 macrophages.	The compound decreased the NO production (IC_{50} 9.56 μM).	[38]
Neurolaena lobata (L.) Cass.	**1)** Neurolenin B **2)** Neurolenin C **3)** Neurolenin D		LPS-stimulated monocytes.	The compounds **1**–**5** are potent inhibitors of TNF-α production **1** (IC_{50} 2.32 μM), **2** and **3** (IC_{50} 1.10 μM), **4** (IC_{50} 0.17 μM), and **5** (IC_{50} 1.30 μM).	[39]
	4) Lobatin B				
	5) 9α-Hydroxy-8β-isovalerianyloxycalyculatolide				
Onopordum illyricum L.	Vernomelitensin		Anti-NF-κB activity was evaluated in the NIH-3 T3-KBF-Luc cell line. The antiSTAT3 activity was analyzed in HeLa-STAT3-luc cell line. The activation of the Nrf2 pathway was analyzed in the HaCaT-ARE-Luc cell line. The protein concentration in the	Vernomelitensin decreased the activity of NF-κB (IC_{50} 3.6 μM), STAT3 (IC_{50} 27.9 μM), and Nrf2 (IC_{50} 1.1 μM) Onopordopicrin decreased the activity of NF-κB (IC_{50} 8.6 μM), STAT3 (IC_{50} 15.3 μM), and Nrf2 (IC_{50} 2.2 μM).	[28]

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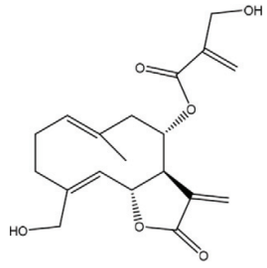
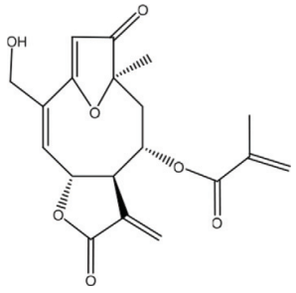
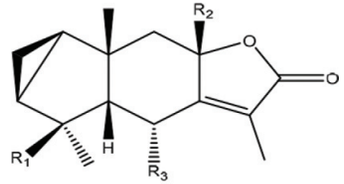
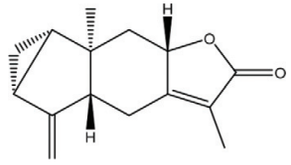
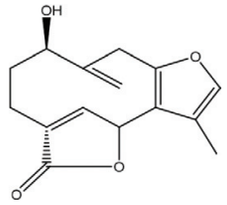
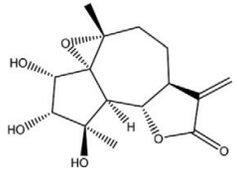
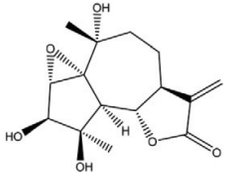
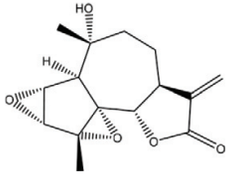
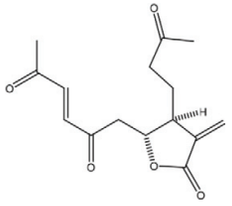
Scientific name	Terpene	Structure	Anti-inflammatory assay	Results	Ref.
	Onopordopicrin		cell extracts were measured by the Bradford method (BioRad).		
Lychnophora passerina (Mart ex DC) Gardner.	Goyazensolide		Carrageenan-induced paw edema assay.	Goyazensolide (10 mg/kg orally) reduced carrageenan-induced paw edema assay in the second hour from the assay. This sesquiterpene lactone presented similar effect to indomethacin.	[40]
Lindera strychnifolia (Sieb. & Zucc.) Fern Vill.	**1)** Linderolide O **2)** Linderolide P **3)** Linderolide Q **4)** Linderolide R	 1) R_1=OCH_3; R_2=H 2) R_1=OH; R_2=OH; R_3=H 3) R_1=OH; R_2=OH;R_3=OH 4) R_1=OH; R_2=OH;R_3=OAc	LPS-stimulated RAW 264.7 macrophages.	The compounds inhibited the NO production with the following IC_{50} values (μM): **1** (6.3), **2** (9.6), **3** (14.6), **4** (12.8), **5** (15.4), **6** (9), and the positive control amino guanidine (18.4).	[41]
	5) Menelloide C				

Scientific name	Terpene	Structure	Anti-inflammatory assay	Results	Ref.
	6) Parvigemone				
Artemisia austroyunnanensis Y. Ling & Y. R. Ling.	**1)** Austroyunnane B		LPS-stimulated RAW 264.7 macrophages.	The compounds inhibited the NO production with the following IC_{50} values (μM): **1** (4.20), **2** (10.67), **3** (5.10), **4** (8.77), **5** (4.21), **6** (2.57), and the positive control L-NMMA (24.95).	[42]
	2) Austroyunnane C				
	3) Austroyunnane D				
	4) Artecaninhydrate				

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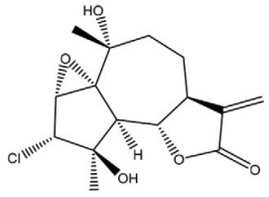
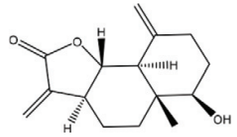
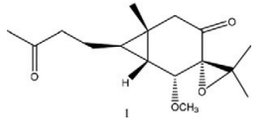
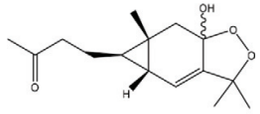
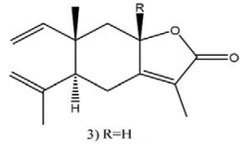
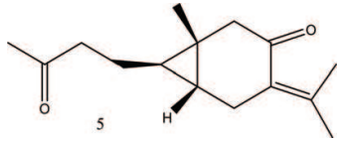
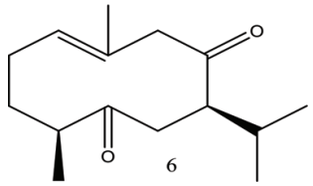
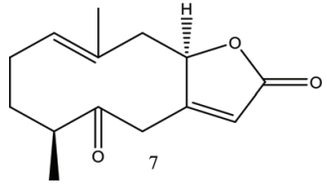
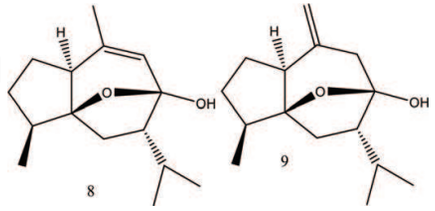
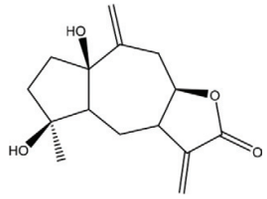
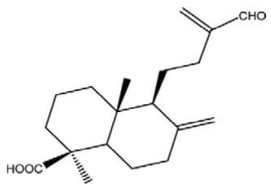
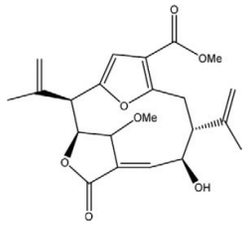
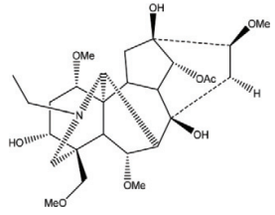
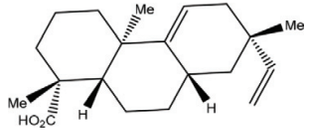
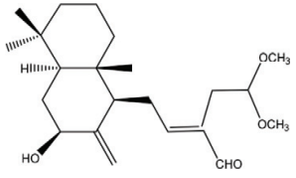
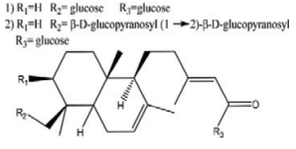
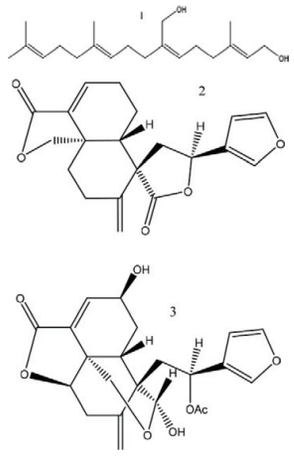
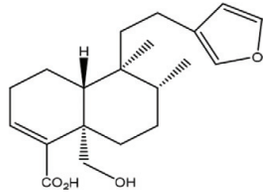
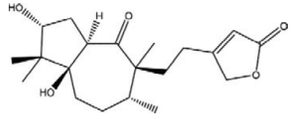
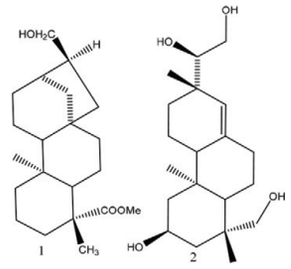
Scientific name	Terpene	Structure	Anti-inflammatory assay	Results	Ref.
	5) 3α- Chloro-4β,10α-dihydroxy-1β,2β-epoxy-5α,7αH-guai-11(13)-en-12,6α-olide				
	6) 15,16-Reynosin				
Curcuma wenyujin Y. H. Chen & C. Ling.	**1)** 7α,11-Epoxy-6α-methoxy-carabrane-4,8-dione **2)** 8,11-Epidioxy-8-hydroxy-4-oxo-6-carabren **3)** Isogermafurenolid **4)** Hydroxyisogermafurenolide **5)** Curcumenone **6)** Neocurdione **7)** Curdionolide B **8)** Isocurcumol **9)** 4-Epicurcumol	 1  2  3) R=H 4) R=OH  5	LPS-stimulated RAW 264.7 macrophages.	The compounds inhibited the NO production with the following IC_{50} values (μM): **1** (47.05), **2** (25.36), **3** (30.62), **4** (59.97), **5** (34.69), **6** (24.18), **7** (14.50), **8** (22.36), **9** (17.26), and the positive control hydrocortisone (64.34).	[43]

Scientific name	Terpene	Structure	Anti-inflammatory assay	Results	Ref.
		 6			
		 7			
		 8 9			
Pulicaria undulata (L.) C.A. Mey.	1β,4β-Dihydroxy-5α*H*,7α*H*,8α-guaia-10(14),11(13)-dien-8α,12-olide		LPS-stimulated RAW 264.7 macrophages.	The compound inhibited the NO production with IC_{50} 7.2 μM.	[44]
Diterpenes					
Thuja orientalis L.	15-nor-14-Oxolabda-8(17),13(16)-dien-19-oic acid		LPS-stimulated RAW 264.7 macrophages.	The compound reduced the expression of iNOS and COX-2 (IC_{50} 1: 3.56 μM). Curcumin was used as a positive control.	[45]

http://dx.doi.org/10.5772/intechopen.73215

Scientific name	Terpene	Structure	Anti-inflammatory assay	Results	Ref.
Pseudopterogorgia acerosa Pallas.	Pseudopterane		LPS-stimulated peritoneal macrophages.	This compound (25 μM) inhibited the expression and secretion of TNF-α, IL-6, IL-1β, NO, IP-10, COX-2 iNOS and monocyte chemoattractant protein-1 (IC_{50} = 12.25).	[46]
Aconitum laciniatum (Brühl) Stapf.	14-*O*-Acetylneoline		TNBS-induced colitis model in mice.	At doses 10, 20 and 50 μg/mouse showed significant protection against different parameters of colitis inflammation.	[47]
Aconitum koreanum Rapaics.	Acanthoic acid		LPS-stimulated RAW 264.7 peritoneal macrophages. Ear edema in mice induced by TPA.	The compound (10 μM) decreased the levels of IL-1β, IL-18, TNF-α, and IFN-γ. Decreased ear edema (0.5 μg/ear), and indomethacin was used as the positive control (0.5 μg/ear).	[48]
Hedychium coronarium J. Koening.	7β-Hydroxycalcaratarin A		Measurement of superoxide anion generation.	Inhibition (IC_{50} 4.52 μg/mL) of superoxide anion generation by human neutrophils.	[49]
Physalis angulata L.	**1)** Physangulatoside A **2)** Physangulatoside F		LPS-stimulated RAW 264.7 macrophages.	Compounds displayed inhibitory effects against NO production with IC_{50} values of 15.9 μM and 60.7 μM, respectively.	[50]

Scientific name	Terpene	Structure	Anti-inflammatory assay	Results	Ref.
Croton stellatopilosus H. Ohba.	**1)** Plaunotol **2)** Plaunolide **3)** Plaunol E		LPS-stimulated RAW 264.7 macrophages.	Plaunotol, plaunolide and plaunol E showed IC_{50} values of 3.41, 17.09, and 2.79 μM, respectively. Plaunotol suppressed expression of the iNOS gene. Plaunolide decreased the expression of the COX-1, COX-2 and iNOS genes. Plaunol E inhibited the expression of the COX-2.	[51]
Dodonaea viscosa Jacq.	Hawtriwaic acid		Kaolin/carrageenan-induced monoarthritis model. Ear edema induced with TPA.	After 10 days of treatment with different doses of hawtriwaic acid (5, 10, 20 mg/kg) decreased knee inflammation in a range of 40–70%. Hawtriwaic acid decreased the levels of proinflammatory cytokines IL-1β, IL-6, and TNF-α.	[20]
Callicarpa randaiensis Hayata.	Randainins D		Measurement of superoxide anion generation.	The compound exhibited moderate inhibition of superoxide anion generation with an IC_{50} value of 21.5 μM.	[52]
Siegesbeckia pubescens (Makino) Makino.	**1)** Methyl *ent*-16α*H*-17-Hydroxy-kauran-19-oate **2)** Kirenol		LPS-stimulated BV2 microglia cells.	Each compound, tested at 100 μM, decreased the expression of iNOS and COX-2 by 20.5% and 22.5%, respectively.	[53]

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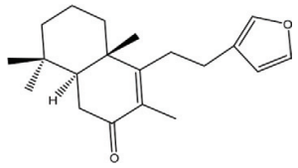
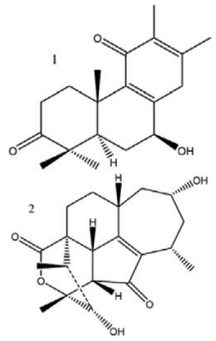
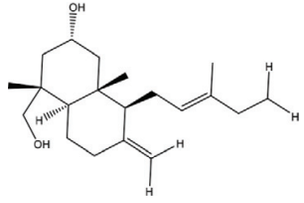
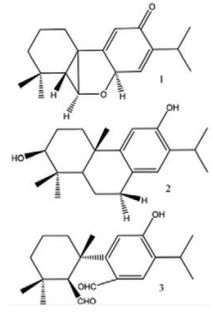
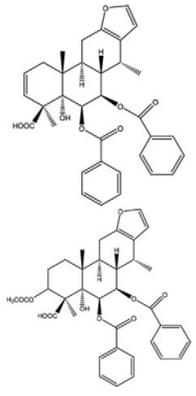
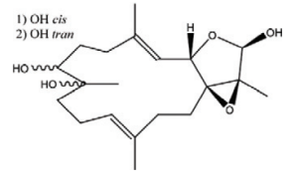
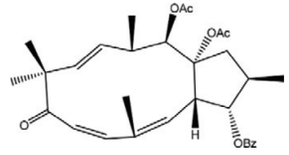
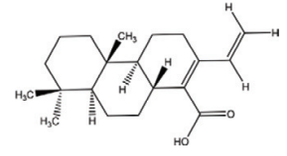
Scientific name	Terpene	Structure	Anti-inflammatory assay	Results	Ref.
Leonurus japonicus Houtt.	Hispanone		Inhibition of superoxide anion generation and elastase release.	The compound decreased the superoxide anion with IC_{50} = 8.48 μM.	[54]
Cephalotaxus lanceolata K.M. Feng.	**1)** Lanceolatins C **2)** Gongshanolide		LPS-stimulated RAW 264.7 macrophages.	The compounds decreased the NO production with IC_{50} values of 10.79 μM and 12.73 μM, respectively. .	[55]
Ocimum labiatum (N.E. Br.) A.J. Paton.	Labda-8(17),12E,14-triene-2R,18-diol		Cytometric bead array (CBA) technique. The effect on phytohemagglutinin (PHA)-induced nitric oxide (NO) production in peripheral blood mononuclear cells (PBMCs) was also assessed.	The compound tested at 25 μg/ml inhibited the production of pro-inflammatory cytokines IL-2, IL-4, IL-6, and IL-17A. The compound decreased the NO production with IC_{50} value of 70 μM.	[56]
Cunninghamia konishii Hayata.	**1)** Konishone **2)** Hinokiol **3)** 12-Hydroxy-6,7-secoabieta-8,11,13-triene-6,7-dial		LPS-stimulated RAW 264.7 macrophages.	The compounds inhibited the NO production with the following IC_{50} values (μM): **1** (9.8), **2** (7.9), and **3** (9.3).	[57]

Scientific name	Terpene	Structure	Anti-inflammatory assay	Results	Ref.
Caesalpinia pulcherrima (L.) Sw.	**1)** Pulcherrimin B **2)** Pulcherrimin D		Evaluated via the oxidative burst assay using a luminol-amplified chemiluminescence technique.	The compounds inhibited the production of reactive oxygen species with IC_{50} values of 15.30 μM and 8 μM, respectively.	[58]
Lobophytum crassum von Merenzeller.	**1)** Lobocrasol A **2)** Lobocrasol B		Were evaluated using NF-kB luciferase and reverse transcription polymerase chain reaction (RT-PCR).	Significantly inhibited TNF-α induced NF-kB transcriptional activity in HepG2 cells in a dose-dependent, with IC_{50} values of 6.30 and 6.63 μM.	[59]
Euphorbia helioscopia L.	Jatrophane		LPS-stimulated BV-2 microglial cells.	The compound inhibited the NO production (IC_{50} = 73.7 μM).	[60]
Erythrophleum ivorense A. Chev.	Erythroivorensin		The carrageenan paw edema model in chicken.	The compound (300 mg/kg orally) showed anti-inflammatory effect with similar activity compared to diclofenac (100 mg/Kg).	[61]

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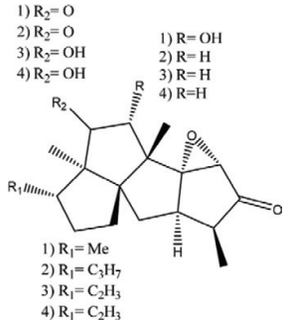
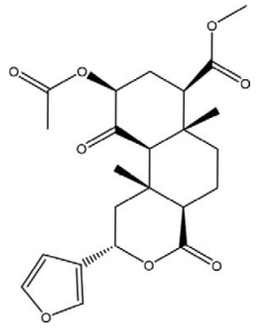
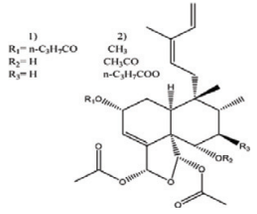
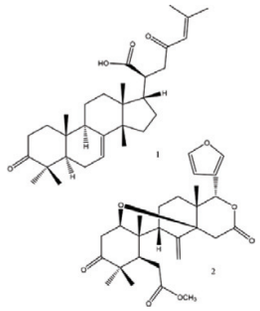
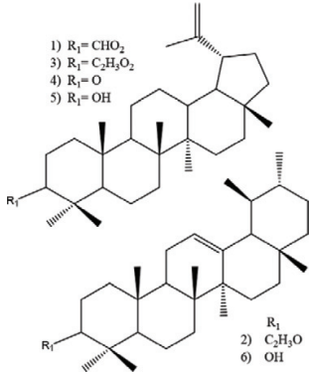
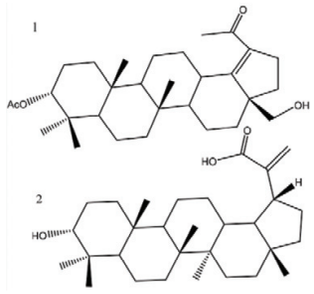
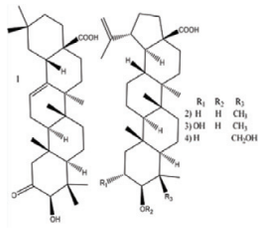
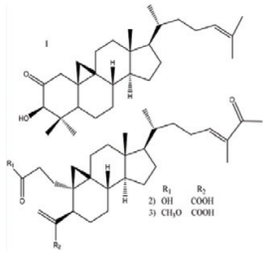
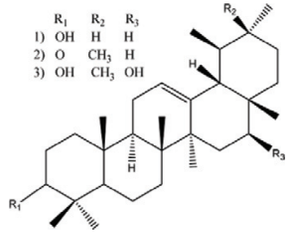
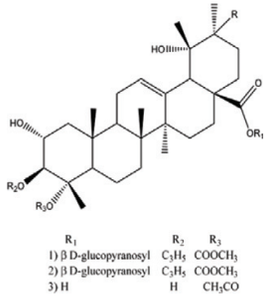
Scientific name	Terpene	Structure	Anti-inflammatory assay	Results	Ref.
Crinipellis species.	**1)** Crinipellin E **2)** Crinipellin F **3)** Crinipellin G **4)** Crinipellin H		LPS/IFN-γ induced CXCL10 promoter activity in transiently transfected human MonoMac6 cells.	Reduce the inducible expression of pro-inflammatory genes in LPS/IFN-γ stimulated human MonoMac6 cells (IC_{50} values of 15, 1.5, 1.3, and 3.15 μM, respectively).	[62]
Salvia divinorum Epling & Játiva.	Salvinorin A		Calcium ionophore-stimulated peritoneal macrophages, and in carrageenan-induced pleurisy in rats.	Inhibited the production of leukotrienes. In carrageenan-induced pleurisy in rats, Salvinorin A significantly inhibited LTB_4 production in the inflammatory exudates, along with reducing the phlogistic process in the lung.	[63]
Casearia sylvestris Sw.	**1)** Caseargrewiin F **2)** Casearin B		Carrageenan-induced paw edema.	At doses 10 and 100 mg/kg showed a significant reduction of the carrageenan-induced paw edema in rats compared to indomethacin.	[64]

Scientific name	Terpene	Structure	Anti-inflammatory assay	Results	Ref.
Triterpenes					
Anopyxis klaineana Pierre (Engl.).	**1)** 3,23-Dioxotirucalla-7,24-dien-21-oic acid **2)** Methyl angolensate		The PGE_2 assay method, sequential competitive enzyme immunoassay with RAW 264.7.	The IC_{50} values were 3.63 μM and 10.23 μM for compounds **1** and **2**, respectively. Cortisone was used as reference standard.	[65]
Bursera copallifera (DC.) Bullock.	**1)** 3-Epilupeol formiate **2)** α-Amyrin acetate **3)** 3-Epilupeol acetate **4)** Lupenone **5)** 3-Epilupeol **6)** α-Amyrin		TPA-induced ear edema in mice, and LPS-stimulated RAW 264.7 macrophages.	The anti-inflammatory effect (1 mg/ear) on ear edema induced by TPA were: **1)** 55.14%, **2)** 62.12%, **3)** 49.35%, **4)** 57.25%, **5)** 66.39, and **6)** 25%. The compounds inhibited the NO production with IC_{50} values (μM): **1** (43.31), **2** (22.57), **3** (31.13), **4** (20.8), **5** (15.5), and **6** (8.98).	[66]
Euonymus carnosus Hemsl.	**1)** 3α-Acetoxy-28-hydroxy-30-norlupane-18(19)-en-20-one **2)** 3α-Hydroxylup-20(29)-en-30-oic acid		LPS-stimulated BV-2 microglial cells.	The compounds inhibited the NO production with IC_{50} values (μM): **1** (5.99) and **2** (8.47).	[67]

http://dx.doi.org/10.5772/intechopen.73215

Scientific name	Terpene	Structure	Anti-inflammatory assay	Results	Ref.
Chaenomeles sinensis (Thouin) Koehne.	**1)** Sinenic A acid **2)** 3β-*O*-cis-Feruloyl-2α,19α-dihydroxy-urs-12-en-28-oic acid **3)** 3β-*O*-cis-caffeoylbetulin **4)** Betulinic acid		LPS-stimulated microglia BV2 cells.	The compounds inhibited the NO production with the following IC_{50} values (μM): **1** (17.8), **2** (4.5), **3** (14.5), and **4** (13.4).	[68]
Gardenia sootepensis Hutch.	**1)** Sootepin F **2)** Sootepin G **3)** Sootepin H		LPS-stimulated macrophages RAW 264.7.	The compounds inhibited the NO production with the following IC_{50} values (μM): **1** (43.6), **2** (18.4), and **3** (15). The compounds inhibited the NF-kB activity with the following IC_{50} values (μM): **1** (20.3), **2** (>100), and **3** (42.3).	[29]
Protium paniculatum Engl.	**1)** α-Amyrin **2)** α-Amyrone **3)** Maniladiol		LPS-stimulated J774A.1 macrophages.	The compounds tested at 1 μg/ml inhibited the NO production by 98.34% **1**), 99.86%, **2**), and 96.05% **3**).	[69]
Quercus serrata var. brevipetiolata (A. DC.) Nakai.	**1)** 3,23-*O*-Methyl butyrate-2,3,19,23-tetrahydroxy-urs-12-en-28-oic acid β-D- glucopyranosyl ester **2)** 3,23-*O*-Methyl butyrate−2,3,19,23-tetrahydroxy-olean-12-en-28-oic acid β-D-glucopyranosyl ester **3)** 23-Acetoxy-2,3,19 - trihydroxyurs-12-en-28-oic acid		LPS-induced NO production and interleukins pro-inflammatory.	The compounds inhibited the NO production with the following IC_{50} values (μM): **1** (8.2) μM, **2** (12.8), and **3** (19.1).	[70]

3. Conclusion

This book chapter indicates that there has been an increase in the search of terpenes with anti-inflammatory activity in recent years. This fact indicates that terpenes are a topic of interest. The possible mechanisms involved in the anti-inflammatory effects of the terpenes are pointing out on the inhibition of NF-κB, TNF-α, PGE2, and pro-inflammatory cytokines such as IL-6. NF-κB is one of the current targets for the development of new anti-inflammatory drugs [71]. In addition, the molecular targets of terpenes are highly desirable to find target-specific anti-inflammatory drugs. The mechanism of action of many terpenes remains to be studied. The combination of terpenes with high anti-inflammatory activity and with studied mechanism of action and currently used drugs could be another strategy for further anti-inflammatory therapy.

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