

Review

Anti-Inflammatory Activity of Alkaloids: An Update from 2000 to 2010

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Abstract: Many natural substances with proven anti-inflammatory activity have been isolated throughout the years. The aim of this review is to review naturally sourced alkaloids with anti-inflammatory effects reported from 2000 to 2010. The assays were conducted mostly *in vivo*, and carrageenan-induced pedal edema was the most used experimental model. Of the 49 alkaloids evaluated, 40 demonstrated anti-inflammatory activity. Of these the most studied type were the isoquinolines. This review was based on NAPRALERT data bank, Web of Science and Chemical Abstracts. In this review, 95 references are cited.

Keywords: alkaloids; anti-inflammatory activity; inflammation; experimental models; review

1. Introduction

Inflammation has been studied for thousands of years. Celsius (in 30 A.D.) described the four classical signs of inflammation (redness, heat, pain, and swelling), and used willow leaf extracts to relieve them [1].

The inflammatory process is a reaction of the body to the penetration of an infectious agent, an antigen, or cell damage. Inflammation is the most frequent sign of disease, and is also a fundamental biological process involving complex pathways that are often induced by the products of bacterial degradation from various microorganisms; lipopeptides, lipopolysaccharides, peptidoglycans, formylmethionyl peptides, flagellin, microbial DNA), fungi (zymosans), viruses (double-stranded RNA), or even the body's own cells upon damage and death [2].

The inflammatory response starts with signal recognition that may have an infectious or inflammatory origin, and the release of chemicals from tissues and migrating cells called mediators [3]. The list of these mediators includes amines like histamine and 5-hydroxytryptamine, bradykinin, (representing short peptides), long peptides such as interleukin-1 (IL-1), lipids such as prostaglandins (PGs) and leukotrienes (LTs), and enzymes [1]. During the immune response, these mediators recruit adjacent cells through the paracrine process. When these mediators exceed local borders, they disseminate, and distribute through the blood, producing endocrine generalized cellular activation, or systematic inflammatory response syndrome (SIRS). SIRS is a host defense mechanism, and part of the tissue repair process. To effectively initiate this defense mechanism, cytokines with pro-inflammatory function are required, such as TNF- α , IL-1 β , interleukin-12 (IL-12), interferon- γ (IFN- γ) and possibly IL-6 [4-7]. The initial inflammatory response is controlled by immune-regulating molecules through specific inhibitors, and soluble cytokine receptors. The main anti-inflammatory cytokines are transforming beta growth factor (TGF- β) and interleukins 4 and 10. Specific receptors for IL-1, TNF- α and interleukin-18 (IL-18) act as inhibitors of their own pro-inflammatory cytokines. Under physiological conditions immune-modulator molecules act to limit the potentially harmful effects of the inflammatory response [3]. The importance of each of these mediators can be seen when it is removed (either by preventing its generation with enzyme inhibitors or by preventing its pharmacological effects with selective antagonists) [1].

In inflammation research, several experimental models have been used to evaluate inflammation. The usual method of determining whether compounds have anti-inflammatory activity is to test them in animal, and biochemical inflammation models. However there is no single experimental model that covers all aspects of inflammation.

Natural products have long been recognized as an important source of therapeutically effective medicines. It is recognized that natural-product structures have great chemical diversity, biochemical specificity, and other molecular properties that make them favorable lead structures [8-13].

Among the 877 small-molecules New Chemical Entities (NCEs) introduced between 1981 and 2002, roughly 49% (~429 molecules) were natural products, semi-synthetic natural product analogues, or synthetic compounds based on natural-products [9], moreover, between 2005 and 2007, 13 natural, product-derived drugs were approved in the United States, with five of them being the first members of new classes [14]. In recent years advances in chemical and pharmacological techniques have contributed to the knowledge of new therapeutically active compounds obtained from natural products [15].

The alkaloids represent the largest single class of plant secondary metabolites. They have a remarkable range of often dramatic pharmacological activity, and are also often toxic to man [16]. Many alkaloids are used in therapeutics and as pharmacological tools. A wide range of biological effects has been reported for alkaloids, including emetic, anti-cholinergic, antitumor, diuretic, sympatho-mimetic, antiviral, antihypertensive, hypno-analgesic, antidepressant, mio-relaxant, anti-tussigen, antimicrobial and anti-inflammatory activities [17-19]. However, alkaloids and other natural compounds are generally complex, making it necessary to analyze their pharmacological activities using several experimental methods and demonstrate their structure/activity correlation. It is common to find pharmacological data where a single experimental model was used to demonstrate a biological activity. However pathological responses are extremely complex involving many biological events, so it is necessary to use different experimental models to define the exactly mechanism of action of the analyzed molecule [20].

In the course of our continuing search for bioactive natural plant products, we have published reviews on crude plant extracts and plant-derived compounds with potential uses [21-37]. Moreover, our group has also reviewed the medicinal and poisonous plants of Northeast Brazil [38,39], among others [40-52]. Recently we published a review on the anti-inflammatory activity of alkaloids reported in the twentieth century, more precisely covering the period from 1907 to 2000 [53]. Now we present an update of the literature on alkaloids with anti-inflammatory activity from 2000 to 2010. The search was carried out on data banks such as Web of Science, Chemical Abstracts, and NAPRALERT (acronym for the University of Illinois Natural Products ALERT service). The references found in the searches were later consulted. For details on the mechanism-based bioassays utilized for anti-inflammatory activity, the original references should be consulted.

2. Results and Discussion

Isoquinoline, quinoline and indole alkaloids were the most studied classes for anti-inflammatory activity. Among the isoquinolines, berberine was the most studied compound, being active in almost all the experimental models described in Table 1. This compound is present in numerous plants of the *Berberis* and *Coptis* genera [54]. It is one of the major components of *Coptis chinensis*, which is frequently utilized in Chinese herbal drugs to treat inflammatory reactions. Berberine has a variety of pharmacologic effects, including inhibition of TPA-induced mouse ear edema, indicating that this alkaloid may have activity against chronic inflammation [55].

Investigations demonstrated that warifteine, a bisbenzylisoquinoline alkaloid isolated from *Cissampelos sympodialis*, inhibits eosinophil recruitment, eotaxin and cisteinyl leukotriene production in the pleural cavities, and lungs of allergic mice, as well as inhibiting in the production of nitric oxide mediators. These data highlight the role of warifteine as a potential anti-allergic and anti-inflammatory molecule [56,57]. Other isoquinoline alkaloids like berbamine, palmatine and columbamine were also examined demonstrating significant dose-dependent inhibitory activity in serotonin-induced hind paw edema assays for both oral and topical applications, and in oral administration, on acetic acid-induced vascular permeability [58].

The quinolizidine alkaloids matrine and oxymatrine, isolated from *Sophora subprostrata* (a Chinese plant used as an antipyretic, antidote, and analgesic) exhibited *in vitro* cyclooxygenase inhibition and antioxidant activity, providing scientific support for their existing medicinal use in traditional Chinese medicine [59].

Indole alkaloids such as brucine and brucine-N-oxide were also reported in this review. They demonstrated significant analgesic and anti-inflammatory properties. Both compounds demonstrated a substantial protective effect in experimental models such as hot-plate test and writhing test. Although, in formalin test, they exhibited their analgesic activity in different phases. In carrageenan-induced rat paw edema experiment, brucine *N*-oxide showed stronger inhibitory effect than brucine. In addition, these two substances have diminished acetic-acid induced vascular permeability and inhibited the release of PGE₂ in inflammatory tissue. These results suggest that brucine and brucine-*N*-oxide have different biochemical mechanisms, in spite of having similar chemical structure [60].

Marine natural products have been the focus for discovery of new chemical and pharmacological products. A bisindolic alkaloid named caulerpin isolated from the lipid extract of the algae *Caulerpa racemosa* exhibited anti-inflammatory activity in mice when given orally at a concentration of 100 µmol/kg [63]. The bisindolic pharmacophoric nucleus of caulerpin is most likely responsible for the wide variety of biological properties tested; anti-inflammatory, antinociceptive [61] insecticidal [62], tumor inhibition [63], and inhibition of hypoxia transcription factor [64], all for this one alkaloid.

Amide alkaloids such as riparin I (*N*-benzoyl tyramine) and II (*N*-(2-hydroxybenzoyl) tyramine), isolated from the unripe fruit of *Aniba riparia* decreased carrageenan-induced paw edema at 4 h and 2 h respectively, when compared to a control [65,66]. It appears that the degree of hydroxylation of the benzoyl moiety increases the anti-inflammatory activity.

Most of the alkaloids reported in this review offer considerable promise as anti-inflammatory compounds or drug candidates and some of them appear to be remarkably active. The results of this search are presented in Table 1 in alphabetical order of their chemical names, followed by the plant species of origin. The references were consulted for details of the experimental models used while testing the alkaloid's anti-inflammation activities (assay, organism tested, dose or concentration, activity, and references).

Table 1. Alkaloids with anti-inflammatory activity.

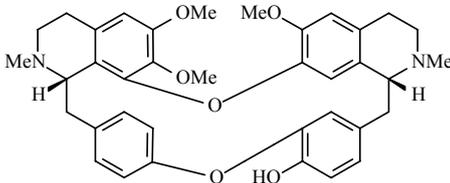
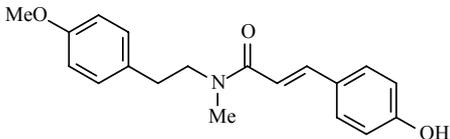
Substance and (Source)	Assay	Organism tested	Dose	Activity	Ref.
Acanthine, oxy (<i>Berberis crataegina</i>)	<i>In vivo</i> , 5-HT-Induced pedal edema	Mouse	200 mg/Kg	Inactive	[58]
	<i>In vivo</i> , 5-HT-Induced pedal edema	Mouse	200 mg/Kg	Active	[58]
Ailanthamide (<i>Zanthoxylum ailanthoides</i>)	<i>In vivo</i> , inhibitory activity on superoxide generation by human neutrophils	Human	IC ₅₀ ≤ 5.34 µg/mL	Active	[67]
	<i>In vivo</i> , inhibitory activity on elastase release by human neutrophils	Human	IC ₅₀ ≤ 5.53 µg/mL	Active	[67]

Table 1. Cont.

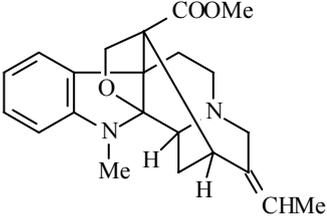
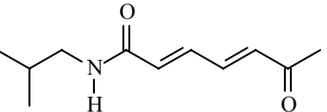
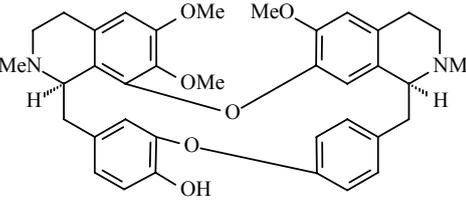
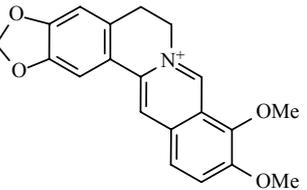
Substance (Source)	Assay	Organism tested	Dose	Activity	Ref.
Akuammigine, pseudo (<i>Picralima nitida</i>)	<i>In vivo</i> , carrageenan-induced pedal edema	Rat	1 mg/Kg	Active	[68]
					
Amide, (2 <i>E</i> ,4 <i>E</i>)- <i>N</i> -isobutyl-6-oxohepta- 2,4-dien (<i>Zanthoxylum ailanthoides</i>)	<i>In vivo</i> , inhibitory activity on superoxide generation by human neutrophils	Human	IC ₅₀ ≤ 5.34 μg/mL	Active	[67]
					
Berberamine (<i>Berberis crataegina</i>)	<i>In vivo</i> , 5-HT-induced pedal edema	Mouse	200 mg/Kg	Active	[58]
					
	<i>In vivo</i> , 5-HT-induced pedal edema	Mouse	100 mg/Kg	Active	[58]
Berberine (<i>Hydrastis canadensis</i> , <i>Coptidis rhizoma</i> , <i>Phellodendri cortex</i> and <i>Berberis crataegina</i>)	<i>In vivo</i> , TNB-induced colitis	Rat	15 mg/Kg	Active	[69]
					
	<i>In vivo</i> , LPS-induced hepatotoxicity	Mouse	100 mg/Kg	Inactive	[70]
	<i>In vivo</i> , carrageenan-induced pedal edema	Mouse	2 mg/Kg	Active	[70]
	<i>In vivo</i> , LPS-induced hepatotoxicity	Mouse	209 mg/Kg	Active	[70]
	<i>In vivo</i> , 5-HT induced-pedal edema	Mouse	200 mg/Kg	Active	[58]
	<i>In vivo</i> , Carrageenan-induced pedal edema	Rat	5 mg/Kg	Active	[55]
	<i>In vivo</i> , acute inflammation induced by <i>E. coli</i> LPS	Chicken	15 mg/Kg	Active	[71]

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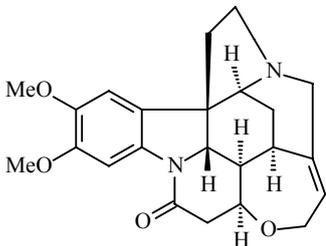
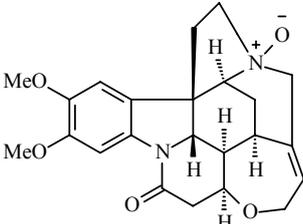
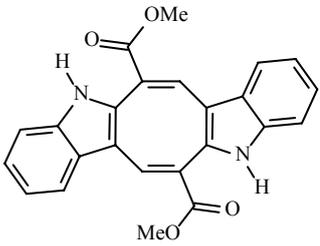
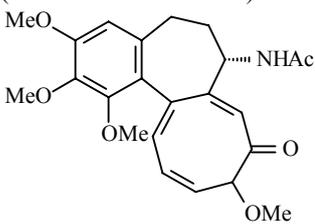
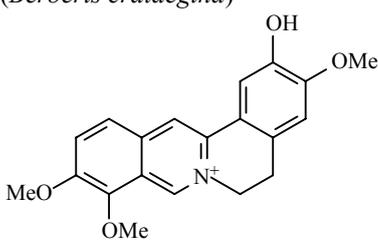
Substance (Source)	Assay	Organism tested	Dose	Activity	Ref.
Brucine (<i>Strychnos nux-vomica</i>)	<i>In vivo</i> , carrageenan-induced pedal edema	Rat	15 mg/Kg	Active	[60]
					
Brucine- <i>N</i> -oxyde (<i>Strychnos nux-vomica</i>)	<i>In vivo</i> , carrageenan-induced pedal edema	Rat	100 mg/Kg	Active	[60]
					
Caulerpin (<i>Caulerpa racemosa</i>)	<i>In vivo</i> , capsaicin-induced ear edema	Mouse	100 μmol/Kg	Active	[61]
					
Colchicine (<i>Colchicum autumnale</i>)	In humans, oral	Human adult	0.5 mg/ person	Active	[72]
					
Columbamine (<i>Berberis crataegina</i>)	<i>In vivo</i> , External, 5-HT-induced pedal edema	Mouse	200 mg/Kg	Inactive	[58]
					
	<i>In vivo</i> , Intragastric, 5-HT-induced pedal edema	Mouse	200 mg/Kg	Inactive	[58]

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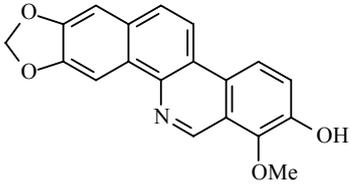
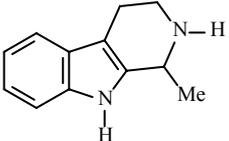
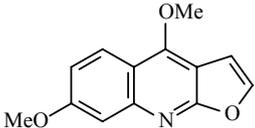
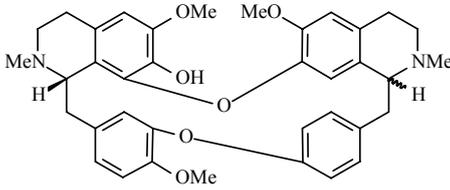
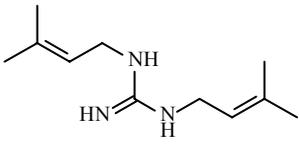
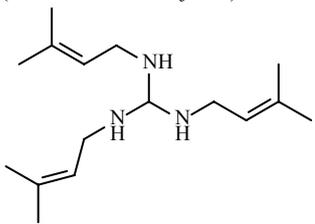
Substance (Source)	Assay	Organism tested	Dose	Activity	Ref.
Decarine (<i>Zanthoxylum ailanthoides</i>)	<i>In vivo</i> , inhibitory activity on superoxide generation by human neutrophils	Human	IC ₅₀ ≤ 5.34 μg/mL	Active	[67]
	<i>In vivo</i> , inhibitory activity on elastase release by human neutrophils	Human	IC ₅₀ ≤ 5.53 μg/mL	Active	[67]
Eleagnine (<i>Chrysophyllum albidum</i>)	<i>In vivo</i> , carrageenan-induced paw edema	Rat	10 mg/Kg	Active	[73]
					
Evolitrine (<i>Evodia lunu-ankeda</i>)	<i>In vivo</i> , carrageenan-induced rat paw edema	Rat	20 mg/Kg	Active	[74]
					
Fangchinoline (<i>Stephania tetrandrae</i>)	<i>In vivo</i> , croton oil-induced edema	Mouse	20 mg/Kg	Active	[75]
	<i>In vivo</i> , croton oil-induced edema	Mouse	0.1 mg/Kg	Active	[75]
	<i>In vitro</i> , fMLP-induced neutrophil adhesion and transmigration	Human	10 μg/mL	Active	[76]
Guanidine, N1,N2-diisopentenyl (<i>Alchornea cordifolia</i>)	<i>In vivo</i> , croton oil-induced ear edema	Mouse	4.2 ± 0.5 mg/Kg	Active	[77]
					
Guanidine, N1,N2,N3-triisopentenyl (<i>Alchornea cordifolia</i>)	<i>In vivo</i> , croton oil-induced ear edema	Mouse	3.7 ± 0.8 mg/Kg	Active	[77]
					

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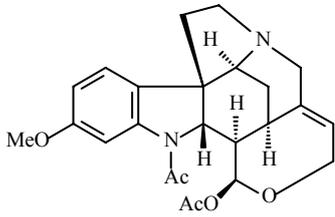
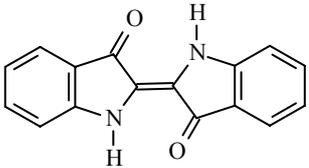
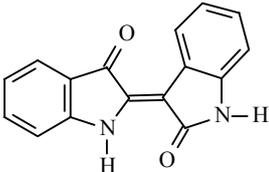
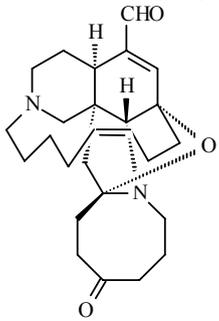
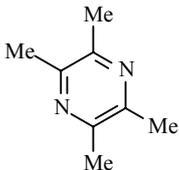
Substance (Source)	Assay	Organism tested	Dose	Activity	Ref.
Henningsamine, 11-methoxy (<i>Strychnos cathayensis</i>)	<i>In vitro</i> , inhibitory activity on superoxide anion generation	Human	IC ₅₀ < 5.5 5.43 ± 1.52 μg/mL	Active	[78]
	<i>In vitro</i> , inhibitory activity on elastase release by human neutrophils	Human	IC ₅₀ < 5.5 3.25 ± 0.31 μg/mL	Active	[78]
Indigo (<i>Indigofera tinctoria</i>)	<i>In vivo</i> , carrageenan-induced pedal edema	Mouse	1 mg/Kg	Active	[79]
					
Indirubin (<i>Indigofera tinctoria</i>)	<i>In vivo</i> , carrageenan-induced pedal edema	Mouse	1 mg/Kg	Active	[79]
					
Ircinal A, 31-keto-12,34-oxa-32,33-dihydro (<i>Acanthostrongylophora</i> sp)	*	*	*	Inactive	[80]
					
Ligustrazine (<i>Ligusticum chuanxiong</i>)	<i>In vitro</i> , macrophages	Human adult	400 mg/L	Active	[81]
	<i>In vivo</i> , carrageenan-induced pedal edema	Rat	50 mg/Kg	Active	[82]
	<i>In vivo</i> , Cotton pellet granuloma	Mouse	50 mg/Kg	Active	[82]

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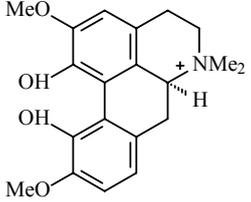
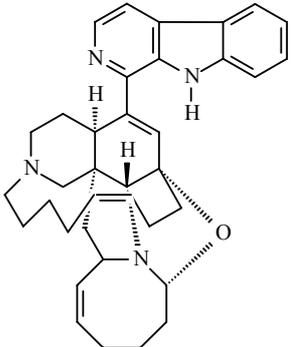
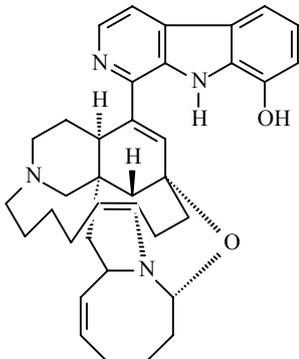
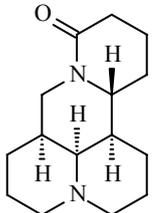
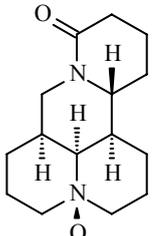
Substance (Source)	Assay	Organism tested	Dose	Activity	Ref.
Magnoflorine (<i>Berberis crataegina</i>)	<i>In vivo</i> , 5-HT-induced pedal edema	Mouse	200 mg/Kg	Inactive	[58]
	<i>In vivo</i> , 5-HT-induced pedal edema	Mouse	200 mg/Kg	Inactive	[58]
Manzamine A, 12,28-Oxa (<i>Acanthostrongylophora</i> sp)	*	*	*	Inactive	[80]
					
Manzamine A, 12,28-oxa-8-hydroxy (<i>Acanthostrongylophora</i> sp)	*	*	*	Inactive	[80]
					
Matrine (<i>Sophora subprostrata</i>)	<i>In vitro</i> , inhibitory activity of COX-1	Rat	31.3 μM	Active	[59]
	<i>In vitro</i> , inhibitory activity of COX-2	Rat	188.5 μM	Moderate activity	[59]
Matrine, oxy (<i>Sophora subprostrata</i>)	<i>In vitro</i> , inhibitory activity of COX-1	Rat	197.8 μM	Moderate activity	[59]
	<i>In vitro</i> , inhibitory activity of COX-2	Rat	385.1 μM	Weak activity	[59]

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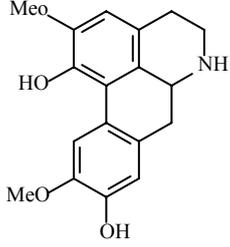
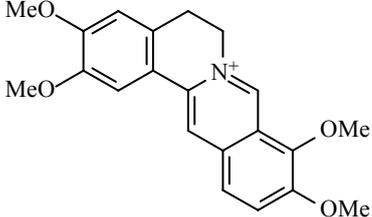
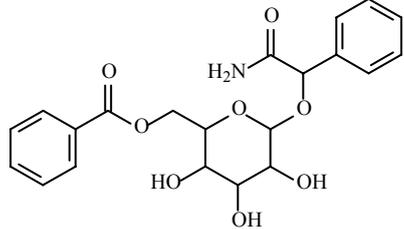
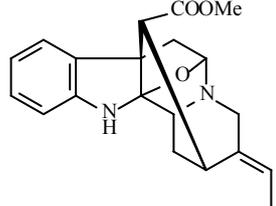
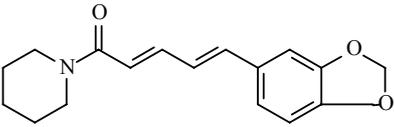
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Norisoboldine (<i>Radix linderae</i>) 	<i>In vivo</i> , collagen II -induced arthritis	Mouse	10 mg/Kg	Active	[83]
Palmatine (<i>Berberis crataegina</i>) 	<i>In vivo</i> , 5-HT-induced pedal edema	Mouse	200 mg/Kg	Inactive	[58]
	<i>In vivo</i> , 5-HT-induced pedal edema	Mouse	100 mg/Kg	Active	[58]
Persicaside (<i>Prunus persica</i>) 	<i>In vitro</i> , inhibitory activity on NO production	Rat	40 µg/mL	Active	[84]
	<i>In vitro</i> , inhibitory activity on PGE ₂ production	Rat	40 µg/mL	Active	[84]
Picrinine (<i>Alstonia scholaris</i>) 	<i>In vitro</i> , inhibitory activity on COX-1	*	100 µM	Inactive	[85]
	<i>In vitro</i> , inhibitory activity on COX-2	*	100 µM	Weak activity	[85]
	<i>In vitro</i> , inhibitory activity on 5-LOX	*	100 µM	Active	[85]
	<i>In vivo</i> , carrageenan-induced air pouch formation	Mouse	10 mg/Kg	Active	[85]
	<i>In vivo</i> , xylene-induced ear edema	Mouse	10 mg/Kg	Active	[85]
Piperine (<i>Piper spp</i>) 	<i>In vivo</i> , intragastric	Rat	20 mg/Kg	Active	[86]

Table 1. Cont.

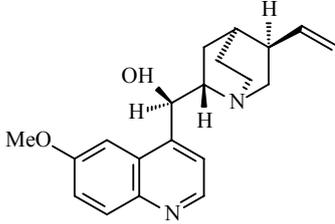
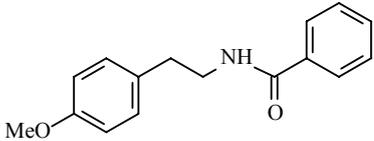
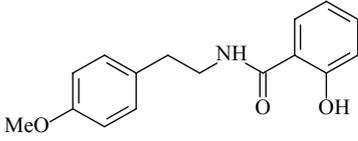
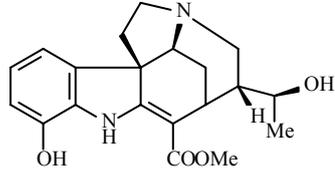
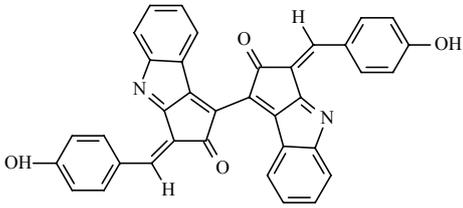
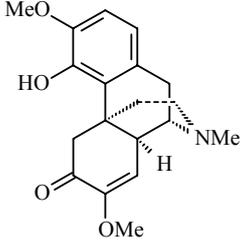
Substance (Source)	Assay	Organism tested	Dose	Activity	Ref.
Quinine (<i>Cinchona</i> spp)	In humans, oral	Human adult	200 mg/day	Inactive	[87]
					
Riparin I (<i>Aniba riparia</i>)	<i>In vivo</i> , formalin test	Mice	25 mg/Kg	Active	[88]
	<i>In vivo</i> , carrageenan-induced pedal edema	Mice	25 mg/Kg	Active	[65]
Riparin II (<i>Aniba riparia</i>)	<i>In vivo</i> , carrageenan-induced pedal edema	Rat	25 mg/Kg	Active	[66]
					
Scholaricine (<i>Alstonia scholaris</i>)	<i>In vitro</i> , inhibitory activity on COX-1	Mice	100 μ M	Active	[85]
	<i>In vitro</i> , inhibitory activity on COX-2	Mice	100 μ M	Active	[85]
	<i>In vitro</i> , inhibitory activity on 5-LOX	Mice	100 μ M	Active	[85]
	<i>In vivo</i> , carrageenan-induced air pouch formation	Mouse	5 mg/Kg	Active	[85]
	<i>In vivo</i> , xylene-induced ear edema	Mouse	5 mg/Kg	Active	[85]
Scytonemin (Extracellular sheath of cyanobacteria)	<i>In vitro</i> , phorbol-induced edema of the mouse ear	Mouse	5–100 μ g/ear	Active	[89]
					
Sinomenine (<i>Sinomenium acutum</i>)	<i>In vivo</i> , collagen II induced arthritis	Rat	3.036 mg/Kg	Active	[90]
					

Table 1. Cont.

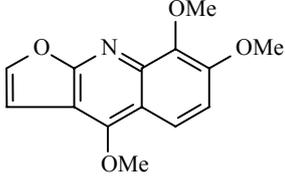
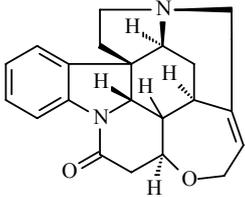
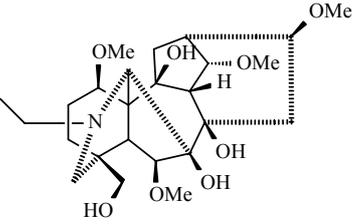
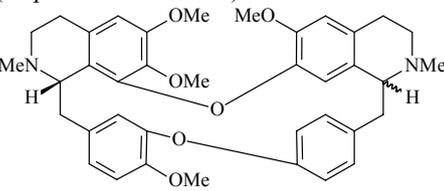
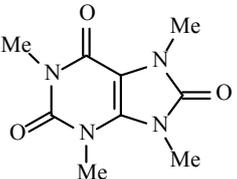
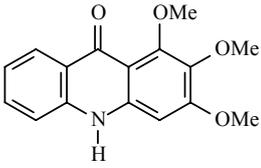
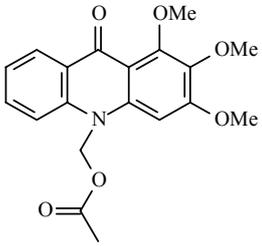
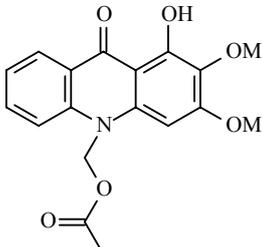
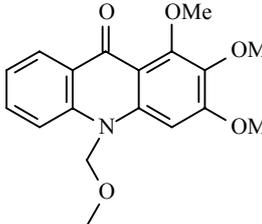
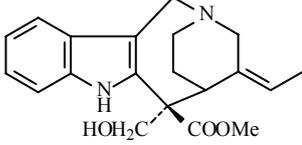
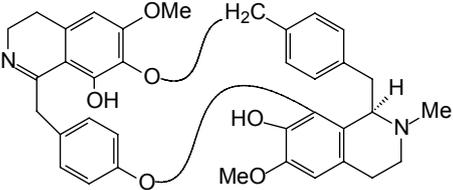
Substance (Source)	Assay	Organism tested	Dose	Activity	Ref.
Skimmiaine (<i>Decatropis bicolor</i>) 	<i>In vivo</i> , TPA-induced inflammation	Mouse	0.75 mg/ear	Active	[91]
Strychnine (<i>Strychnos nuxvomica</i>) 	<i>In vivo</i> , carrageenan-induced pedal edema <i>In vivo</i> , cotton pellet granuloma	Rat Rat	* *	Inactive Inactive	[92] [92]
Swatinine (<i>Aconitum laeve</i>) 	<i>In vitro</i> , colorimetric assay with tetrazolium salt	Blood drawn from healthy volunteers	100 µg/mL	Weak Activity	[93]
Tetrandrine (<i>Stephania tetrandrae</i>) 	<i>In vivo</i> , croton oil-induced edema <i>In vivo</i> , croton oil-induced edema <i>In vitro</i> , FMLP-induced neutrophil adhesion and transmigration	Mouse Mouse Human	20 mg/Kg 0.1 mg/Kg 10 µg/mL	Active Active Active	[75] [75] [76]
Theacrine (<i>Camellia kucha</i>) 	<i>In vivo</i> , xylene-induced ear edema <i>In vivo</i> , acetic acid-induced vascular permeability <i>In vivo</i> , carrageenan-induced paw edema	Mouse Mouse Mouse	8 mg/Kg 16 mg/Kg 8 mg/Kg	Active Active Active	[94] [94] [94]
Toddaliopsin A (<i>Toddaliopsis bremekampii</i>) 	<i>In vitro</i> , zymosan activated human polymorphonuclear leucocytes in a chemoluminescence assay system	Human	IC ₅₀ = 27.3 µg/mL	Weak activity	[95]

Table 1. Cont.

Substance (Source)	Assay	Organism tested	Dose	Activity	Ref.
Toddaliopsin B (<i>Toddaliopsis bremekampii</i>) 	<i>In vitro</i> , zymosan activated human polymorphonuclear leucocytes in a chemoluminescence assay system	Human	IC ₅₀ = 48.3 μg/mL	Weak activity	[95]
Toddaliopsin C (<i>Toddaliopsis bremekampii</i>) 	<i>In vitro</i> , zymosan activated human polymorphonuclear leucocytes in a chemoluminescence assay system	Human	IC ₅₀ = 4.21 μg/mL	Active	[95]
Toddaliopsin D (<i>Toddaliopsis bremekampii</i>) 	<i>In vitro</i> , zymosan activated human polymorphonuclear leucocytes in a chemoluminescence assay system	Human	IC ₅₀ = 79.1 μg/mL	Weak activity	[95]
Vallesamine (<i>Alstonia scholaris</i>) 	<i>In vitro</i> , inhibitory activity on COX-1	Mice	100 μM	Active	[85]
	<i>In vitro</i> , inhibitory activity on COX-2	Mice	100 μM	Active	[85]
	<i>In vitro</i> , inhibitory activity on 5-LOX	Mice	100 μM	Active	[85]
	<i>In vivo</i> , carrageenan-induced air pouch formation	Mouse	8 mg/Kg	Active	[85]
	<i>In vivo</i> , xylene-induced ear edema	Mouse	8 mg/Kg	Active	[85]
Warifteine (<i>Cissampelos sympodialis</i>) 	<i>In vivo</i> , allergic eosinophilia and cysteinyl leukotrienes production	Mice	50 μg/animal	Active	[56]
	<i>In vitro</i> . OVA-sensitized animals were evaluated. The response was related with the increase of NO production	Mice	0.4–10 mg/Kg	Active	[57]

* Data incomplete, derived from an abstract.

3. Conclusions

Of the 49 alkaloids evaluated, 40, among which the isoquinolines figured most prominently, demonstrated anti-inflammatory activity. Carrageenan-induced pedal edema was the most utilized experimental model for evaluating anti-inflammatory activity. In this review, 95 references were cited.

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