



Genus *Kalanchoe* (Crassulaceae): A Review of Its Ethnomedicinal, Botanical, Chemical and Pharmacological Properties

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Authors' contributions

Authors may use the following wordings for this section: This work was carried out in collaboration between all authors. All authors read and approved the final manuscript.

Review Article

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ABSTRACT

Genus *Kalanchoe* comprises hundred species. Different extracts of these *Kalanchoe* species have been widely used in traditional medicine. Recently it has been reported that *Kalanchoe* extracts possess various biological activities viz. antiviral, sedative, antiulcer, immunomodulatory, antileishmanial, CNS depressant, anti-inflammatory, thyroid peroxidase inhibitor, cytotoxic, hepatoprotective, antioxidant, analgesic, anticonvulsant, antimicrobial, inhibition of B cell development, cardiovascular, antihyperglycemic, acetylcholinesterase inhibition, insecticidal and larvicidal activities. Earlier studies on different *Kalanchoe* species have reported the isolation of polysaccharides, flavonoids, sterols, ascorbic acid, trace elements, organic acids, hydrocarbons, triterpenoids, phenolic components and bufadenolides. This review presents the botany, chemistry, traditional uses and pharmacological data of genus *Kalanchoe*.

Keywords: *Kalanchoe*; *crassulaceae*; *cytotoxic*; *flavonoids*; *cardiac glycosides*; *triterpenes*.

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1. INTRODUCTION

Kalanchoe is a genus belonging to family Crassulaceae; closely related to Saxifragaceae from which it differs in the regular numerical plan, almost constantly separate ovaries and predominately fleshy habit. Family Crassulaceae is widely distributed for horticulture. *Kalanchoe* comprises hundred species that are native to tropical areas, Africa and Brazil [1, 2, 3, 4, 5]. Other names of genus *Kalanchoe* are *Bryophyllum* and *Cotyledon* [6]. Amongst which are species *K. pinnata* Lam.; *K. brasiliensis* Larranaga; *K. diagremontiana* R. Hamet; *K. spathulata* DC.; *K. gracilis* Hance; *K. streptantha* Baker; *K. blossfeldiana* Poelln.; *K. tubiflora* Raym. Hamet.; *K. angolensis* N. E. Br; *K. bentii* C. H. Wright; *K. diversa* N. E. Br; *K. dyeri* N. E. Br; *K. elizae* Berger; *K. felthamensis* Hort.; *K. kewensis* Hort; *K. latisejala* N. E. Br.; *K. luciae* Hamet; *K. magnidens* N. E. Br.; *K. prasina* N. E. Br.; *K. somaliensis* Baker; *K. sexangularis* N. E. Br.; *K. flammea* Stapf; *K. kirkii* N. E. Br.; *K. glaucescens* Birt.; *K. rotundifolia* Haw.; *K. carnea* Mast.; *K. laciniata* DC; *K. laxiflora* Baker, *K. marmorata* Baker and *K. verticillata* Elliot; those are the most cited in literature [7,8].

2. ETHNOMEDICINAL OR TRADITIONAL USES

The juice of *Kalanchoe* is used for the local treatment of periodontal disease, cheilitis, cracking lips in children, bruises, wounds, boils in Brazil [9], insect bites in India and Srilanka [10], ear infection, dysentery in Nigeria [11], fever, abscesses, coughs, skin diseases and cytotoxic activity [12], cholera, urinary diseases, whitlow in Africa and Asia [13], tissue injuries in Taiwan [14], arthritis and gastric ulcers [10]. Crushed leaves are rubbed on or tied to the head to bring relief for headache in Africa [11], rheumatism in Indonesia [15], treatment of pulmonary infection, rheumatoid arthritis, immunomodulatory and gastric ulcers [16].

3. BOTANICAL DESCRIPTION

Family Crassulaceae or orpine family, stonecrop family, Synonym: Sedaceae, is a large family of dicotyledons, consisting mainly of succulent herbs, but tending to be miniature shrubs or trees in certain genera and species. Most members of the family are remarkable for their xeromorphic structure, particularly the occurrence of water storage tissue in the leaf and stem. Some are believed to be capable of absorbing water directly from the air by special hairs, epidermal cells or adventitious roots. Members of this family are not considered as important crop plants, but they are used for horticulture; many members have an unusual attractive appearance, and are quite hardy, typically needing only minimal care. Succulent glasshouse herbs or subshrubs, with interesting foliage and flowers. Usually robust erect plants; leaves opposite, fleshy, sessile or stalked, varying from entire to crenate and pinnatifid; flowers yellow, purple or scarlet. Terminal paniculate cymes, rather large and often showy; calyx 4 parted, the narrow lobes shorter than the corolla-tube, usually falling early; corolla 4 parted and mostly spreading, the tube usually cup-shaped; 8 stamens and 4 carpels [7].

The leaf usually centric or intermediate between dorsiventral and centric; typical palisade tissue rare, opposite, or alternate, exstipulate. Hairs are usually infrequent, but several kinds recorded; bladder-like hairs sometimes described as epidermal cells; glandular hairs with short or long stalks and which sometimes secrete mucilage; three armed, pointed hairs; biseriate hairs forming a cobweb-like surface to the leaf, together with transitions between these and glandular shaggy types. The leaf surface often covered by a bluish-white coating

of wax secreted from the epidermis. The epidermis is usually composed of cells elongated transversely to the longitudinal axis of the leaf; papillose in a few species. Stomata are present on all parts of the surface of the leaf; surrounded by a girdle of 3 subsidiary cells. Hydathodes, which appear as small pits or spots on the leaf visible to the naked eye, are variously distributed in different species, sometimes covering the whole of both surfaces, at others confined to one surface or arranged in rows near the leaf margin on both surfaces or only on the lower surface. Secretory cells, with apparently tanniferous contents, common in unligified tissues, especially around the veins; only rarely morphologically differentiated from neighbouring cells. Crystals common, solitary, clustered, or in the form of sphaerites and crystal sand [7,17].

The stem is a fleshy structure due to the well developed parenchymatous or collenchymatous tissues of the cortex and pith. Cork usually consisting of thin-walled cells, arising in the epidermis but sometimes sub-epidermal or even more deeply seated in other genera as becoming impregnated with resin and forming a thick layer capable of reducing evaporation in certain species of *Kalanchoe* from Madagascar namely *K. crenata*. Cortex well developed, fleshy; consisting wholly of parenchyma or with the outer part collenchymatous. Centric, sometimes numerous cortical bundles with central xylem present in certain genera. Phloem poorly developed, including narrow sieve tubes which are not easily seen. Xylem nearly always in the form of a continuous cylinder, only rarely dissected by wide rays [7,17].

The root is described as having red root tips, colored by an anthocyan pigment which is intensified by bright light [7,17].

The flowers are bisexual, rarely unisexual then dioecious, actinomorphic, 3- 4- to 5- merous; sepals free or united into a tube, persistent; petals as many as the sepals, free or united; stamens hypogynous or epipetalous, as many as the petals or twice as many; filaments free or adnate to the petals; scale like nectaries usually present between the stamens and carpels. Carpels are superior, equal in number to the petals, free or slightly connate at the base, monolocular; numerous ovules; style is short or elongate [1]. The flowers are generally arranged in cymose inflorescences at the end of the leaf-shoot, or in lateral cymes. They form dichasia with a tendency to pass into monochasia, or are purely monochasial. Dichasia and monochasia may be arranged in racemes, corymbs, umbels or panicles [18]. The fruit is follicular; seeds are minute and elongated; embryo is straight and endosperm is present [1].

4. CHEMICAL PHYTOCONSTITUENTS

A number of authors have isolated and identified several compounds from different *Kalanchoe* species. These compounds may be classified into several groups namely: flavonoid glycosides, anthocyanins, coumarins, bufadienolides, triterpenoids, phenanthrenes, sterols, fatty acids and kalanchosine dimalate salt.

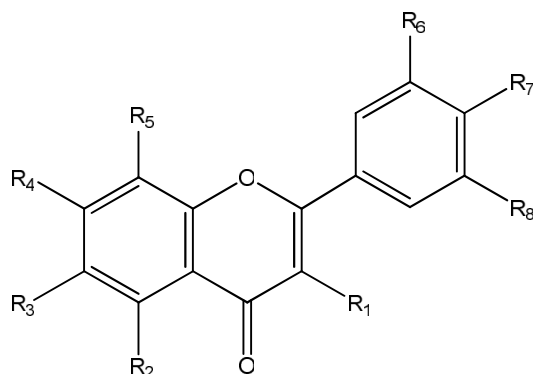
4.1. Flavonoid Glycosides

Published data concerning the isolation & structural elucidation of flavonoid glycosides [5, 14, 19, 20, 21, 22, 23, 24, 25, 26] from different organs of the aforementioned *Kalanchoe* species are summarized in Table 1 & 2.

Table 1. Flavonoids isolated from Genus *Kalanchoe*

Compound Name	Compound No.	Species	Part used	Reference
Patuletin-3,7-di-O-rhamnoside	1	<i>K. spathulata</i>	Leaves & flowers	[5]
Patuletin	2			
Quercetin	3			
Quercetin-3-O-glucoside-7-O-rhamnoside	4			
Kaempferol	5			
Kaempferol-3-O-rhamnoside	6			
Eupafolin-4'-O-rhamnoside	7	<i>K. gracilis</i>	Aerial parts	[14]
Eupafolin-3-7 di-O-rhamnoside	8			
Eupafolin-3-O-rhamnosyl-7-O-(4-O-acetyl-rhamnoside)	9			
Eupafolin-3-O-(3-O-acetyl-rhamnosyl)-7-O-(3-O-acetyl-rhamnoside)	10			
Luteolin	11			
Quercetin	3			
Quercitrin	12			
Kaempferol	5			
Eupafolin	13			
Patuletin-3-O-(4"-O-acetyl- α -L-rhamnopyranosyl)-7-O-(2"-O-acetyl- α -L-rhamnopyranoside)	14	<i>K. brasiliensis</i>	Juice of fresh stems & leaves	[19]
Patuletin-3-O- α -L-rhamnopyranosyl-7-O-(2"-O-acetyl- α -L-rhamnopyranoside)	15			
Patuletin-3-O-(4"-O-acetyl- α -L-rhamnopyranosyl)-7-O-rhamnopyranoside	16			
4"-acetylsagittatin A	17	<i>K. streptantha</i>	Leaves	[20]
Quercetin	3	<i>K. blossfeldiana</i>		[21]
Quercetrin	12			
Quercetin-3-O- β -D-glucoside	18			
Quercitrin	12	<i>K. pinnata</i>	Fresh leaves	[22]
Kapinnatoside	19			
Quercetin-3-O- α -L-arabinopyranosyl (1 \rightarrow 2) α -L-rhamnopyranoside	20			

8-methoxyquercetin-3,7-di-O-rhamnopyranoside	21	<i>K. brasiliensis</i> , <i>K. pinnata</i> & <i>K. gastonis-bornieri</i>	Extracts	[23]
8-methoxykaempferol-3,7-di-O-rhamnopyranoside	22			
Isorhamnetin-3-O- α -L- ¹ C ₄ -rhamnopyranoside	23	<i>K. marmorata</i>	Leaves	[24]
Quercetin	3			
4'-methoxy-myricetin-3-O- α -L- ¹ C ₄ -rhamnopyranoside	24			
Quercitin -3-O- β -D- ⁴ C ₁ -glucopyranoside	18			
Kaempferitrin	25	<i>Bryophyllum pinnatum</i>		[25]
Kaempferol 3-O- α -L-(2-acetyl)rhamnopyranoside-7-O- α -L-rhamnopyranoside	26			
Kaempferol 3-O- α -L-(3-acetyl)rhamnopyranoside-7-O- α -L-rhamnopyranoside	27			
Kaempferol 3-O- α -L-(4-acetyl)rhamnopyranoside-7-O- α -L-rhamnopyranoside	28			
Kaempferol 3-O- α -D-glucopyranoside-7-O- α -L-rhamnopyranoside	29			
Afzelin	30			
α -rhamnoisorobin	31			
3',4'-dimethoxy quercetin	32	<i>K. pinnata</i>	Leaves	[26]

Table 2. Chemical Structures of Flavonoids Isolated from Genus *Kalanchoe*

Compound #	R ₁	R ₂	R ₃	R ₄	R ₅	R ₆	R ₇	R ₈
1	O-rhamnoside	OH	OCH ₃	O-rhamnoside	H	OH	OH	H
2	OH	OH	OCH ₃	OH	H	OH	OH	H
3	OH	OH	H	OH	H	OH	OH	H
4	O-glucoside	OH	H	O-rhamnoside	H	OH	OH	H
5	OH	OH	H	OH	H	H	OH	H
6	O-rhamnoside	OH	H	OH	H	H	OH	H
7	OH	OH	OCH ₃	OH	H	H	O-rhamnoside	H
8	O-rhamnoside	OH	OCH ₃	O-rhamnoside	H	H	OH	H
9	O-rhamnoside	OH	OCH ₃	4-O-acetyl rhamnoside	H	H	OH	H
10	3-O-acetyl rhamnoside	OH	OCH ₃	3-O-acetyl rhamnoside	H	H	OH	H
11	H	OH	H	OH	H	OH	OH	H
12	O-rhamnoside	OH	H	OH	H	OH	OH	H
13	OH	OH	OCH ₃	OH	H	H	OH	H
14	4"-O-acetyl rhamnoside	OH	OCH ₃	2"-O-acetyl rhamnoside	H	OH	OH	H
15	O-rhamnoside	OH	OCH ₃	2"-O-acetyl rhamnoside	H	OH	OH	H
16	4"-O-acetyl rhamnoside	OH	OCH ₃	O-rhamnoside	H	OH	OH	H
17	O-xylose (1 rhamnoside	2) OH →	H	O-acetyl rhamnoside	H	H	OH	H
18	O-glucoside	OH	H	OH	H	OH	OH	H
19	O-arabinoside (1 rhamnoside	2) OH →	H	OH	H	H	OH	H
20	O-arabinoside (1 rhamnoside	2) OH →	H	OH	H	OH	OH	H
21	O-rhamnoside	OH	H	O-rhamnoside	OCH ₃	OH	OH	H
22	O-rhamnoside	OH	H	O-rhamnoside	OCH ₃	H	OH	H
23	O-rhamnoside	OH	H	OH	H	OCH ₃ OH	OH	H
24	O-rhamnoside	OH	H	OH	H	OH	OCH ₃	OH
25	O-rhamnoside	OH	H	O-rhamnoside	H	H	OH	H
26	O-2 acetyl rhamnoside	OH	H	O-rhamnoside	H	H	OH	H
27	O-3 acetyl rhamnoside	OH	H	O-rhamnoside	H	H	OH	H
28	O-4 acetyl rhamnoside	OH	H	O-rhamnoside	H	H	OH	H
29	O-glucoside	OH	H	O-rhamnoside	H	H	OH	H
30	O-rhamnoside	OH	H	OH	H	H	OH	H
31	OH	OH	H	O-rhamnoside	H	H	OH	H
32	OH	OH	H	OH	H	OCH ₃ OCH ₃	H	H

4.2 Anthocyanins

Kalanchoe blossfeldiana varieties with orange, pink, red and magenta flowers contain 3, 5-O- β -D-diglucosides of pelargonidin, cyanidin, peonidin, delphinidin, petunidin and malvidin. Orange varieties contained delphinidin derivatives [21].

4.3 Coumarins

5-hydroxycoumarin was isolated from the aerial parts of *K. gracilis* [14].

4.4 Bufadienolides

Genus *Kalanchoe* is reported to contain plant cytotoxic bufadienolides [12, 15, 27,28,29,30, 31]. The isolated bufadienolides from leaves and whole aerial parts from different *Kalanchoe* species are reported in Table 3, Figure 1.

Table 3. Bufadienolides isolated from Genus *Kalanchoe*

Compound Name	Compound #	Species	Part used	Reference
Hellibrigenin-3-acetate	33	<i>K. lanceolata</i>	Leaves	[27]
Bersaldegenin-1,3,5-orthoacetate	34	<i>K. daigremontiana</i> <i>K. tubiflora</i>	Leaves	[28]
Daigremontianin	35			
Bryophyllin B	36	<i>Bryophyllum pinnatum</i>	Leaves	[29]
Bryophyllin A (Bryotoxic C)	37	<i>K. pinnata</i>	Leaves	[30]
Bryophyllin C	38	<i>K. daigremontiana</i> <i>*tubiflora</i>	Leaves	[15]
Bersaldegenin-1,3,5-orthoacetate	34			
Bryophyllin A	37			
Bryophyllin C	38			
Daigremontianin	35			
Methyl Daigremontate	39			
Bersaldegenin-3-orthoacetate	40			
Bersaldegenin-1-orthoacetate	41			
Kalanchoside A	42	<i>K. gracilis</i>	Aerial parts	[31]
Kalanchoside B	43			
Kalanchoside C	44			
Kalanhybrin A	45	<i>K. hybrida</i>	Whole plant	[12]
Kalanhybrin B	46			
Kalanhybrin C	47			
Daigredorigenin-3-acetate	48			

4.5 Phenolic Acids and Megastigmane

p-Methoxy benzoic acid, *p*-hydroxybenzaldehyde, vanillic acid, *p*-hydroxybenzoic acid, cinnamic acid and nicotinic acid were isolated from the methanol extracts of *K. hybrida* [12]. Protocatechuic-4'-O- β -D-⁴C₁-glucopyranoside was isolated from the ethyl acetate fraction of the leaf aqueous extract of *K. marmorata* [24]. Blumenol A, a megstigmane derivative, was isolated from the methanol extracts of *K. hybrida* [12].

4.6 Sterols, Triterpenes and Phenanthrenes

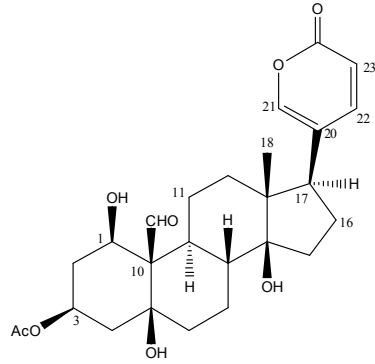
Several compounds had been isolated from the fresh leaves of *Bryophyllum pinnatum*, namely bryophyllol, bryophollone and bryophollenone, bryophynol and 18 α -oleanane, ψ -taraxasterol, along with a mixture of α - and β -amyrins and their acetates [13] and from the whole aerial parts 5 α -stigmast-24-en-3 β -ol; 25-methyl-5 α -ergost-24(28)-en-3 β -ol; (24*R*)-stigmasta-5,25-dien-3 β -ol (24-epiclerosterol) and (24*R*)-5 α -stigmasta-7,25-dien-3 β -ol were isolated [32]. On the other hand, 3-oxo-olean-12-ene and β -sitosterol had isolated from the dichloromethane fraction of the leaves of *K. thrysiflora* [33].

4.7 Organic Salts

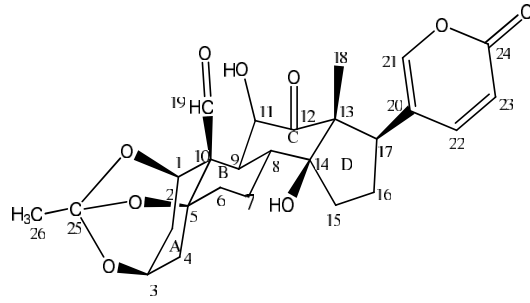
Kalanchosine dimalate (KMC) is an anti-inflammatory salt from the fresh juice of the aerial parts of *Kalanchoe brasiliensis* [34].

4.8 Fatty Acids

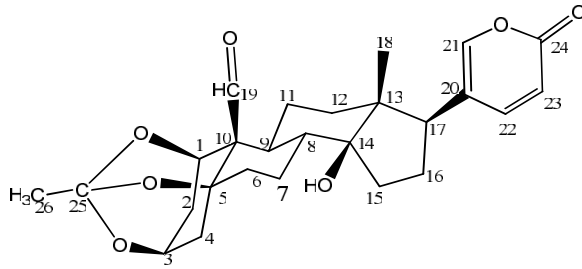
Palmitic acid (C16), stearic acid (C18) and traces of arachidic (C20) and behenic acids (C22) were identified from the ethanol extract of *Kalanchoe pinnata* [35].



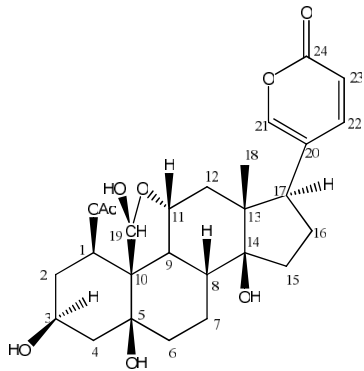
Hellibrigenin-3-acetate 33



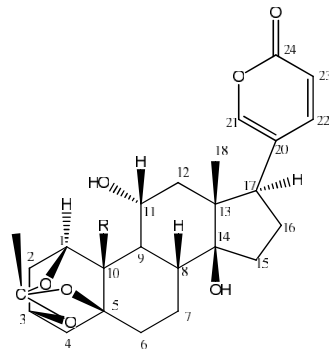
Daigremontianin 35



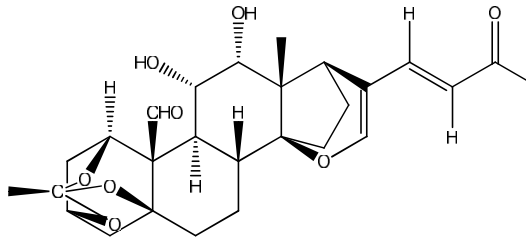
Bersaldeginin-1, 3, 5-orthoacetate 34



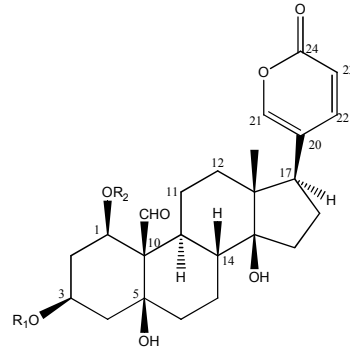
Bryophyllin B 36



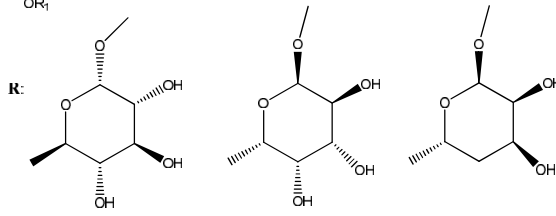
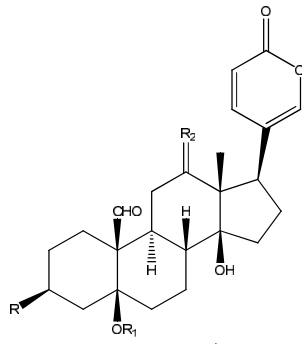
Bryophyllin A, R=CHO 37
Bryophyllin C, R=CH₂OH 38



Methyl diagremonate 39



Bersaldegenin-3-acetate, R₁=Ac; R₂=H 40
Bersaldegenin-1-acetate, R₁=H; R₂=Ac 41



R ₁	H	H	H
R ₂	H ₂	H ₂	O

Kalanchoside A 42

Kalanchoside B 43

Kalanchoside C 44

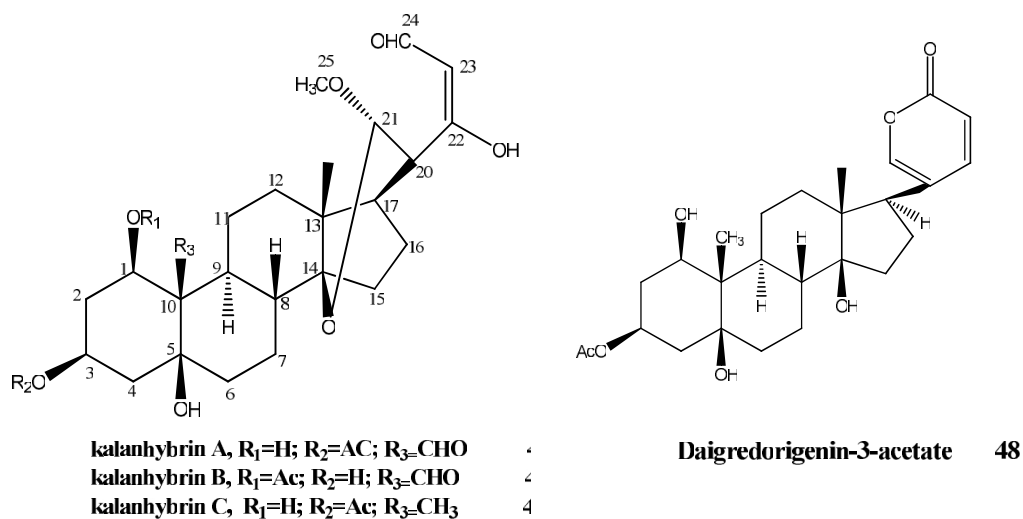


Fig. 1. Structure of Bufadienolides isolated from Genus *Kalanchoe*

5. PHARMACOLOGICAL PROPERTIES

A review of literature revealed that genus *Kalanchoe* had several pharmacological activities viz antiviral, sedative, antiulcer, immunomodulatory, antileishmanial, CNS depressant, anti-inflammatory, thyroid peroxidase inhibitor, cytotoxic, hepatoprotective, antioxidant, analgesic, anticonvulsant, antimicrobial, B cell development inhibitor, cardiovascular activity, antihyperglycemic, larvicidal and insecticidal.

5.1 Antiviral Activity

The antiviral properties of the juice of 8 species belonging to the genera *Kalanchoe*, viz *K. daigremontiana*; *K. petersii*; *K. prolifera*; *K. marnieriana*; *K. blossfeldiana*; *K. beharensis*; *K. waldheimii* and *K. pinnata* were tested. Only the juice from the 4 latter species had shown high virus neutralizing activity [36].

5.2 Sedative Activity

Both bufadienolides viz daigremontianin and bersaldegenin- 1, 3, 5- orthoacetate that were isolated from *K. daigremontiana* and *K. tubiflora* had shown a strong sedative effect in mice at low doses (motility test) and become toxic at higher concentration, inducing paralysis and spasmodic muscle contraction [28].

5.3 Antiulcer Activity

The methanol fraction from the leaf extract of *Bryophyllum pinnatum* possessed significant anti-ulcer activity in nine different experimental animal models. Treating the rats with the methanol extract before the experiment had shown an obvious effect of protection against different ulcerogenic compounds and stress conditions too. Significant protection with extract

treatment was observed to occur for aspirin-induced ulcer in pylorus-ligated rats and for histamine-induced duodenal lesions in guinea pigs [37].

5.4 Immunomodulatory Activity

The aqueous extract of *K. pinnata* leaves showed significant inhibition of cell-mediated and humoral immune responses in mice in a model where spleen cells of animals were pre-treated with *K. pinnata* leaf extract. A delayed-type hypersensitivity reaction to ovalbumin had been developed by intravenous and topical routes followed by intraperitoneal and oral routes. These indicated that the aqueous extract of *K. pinnata* possesses an immunosuppressive activity [10]. The fractionation of the juice of the fresh stems and leaves of *K. brasiliensis* was monitored by an assay measuring lymphocyte proliferation [19]. Recently, the protective effect of the leaves of *K. pinnata* in fatal anaphylactic shock, likewise a Th2 type T cell-driven immunopathology were reported. Oral protection *in vivo* was accompanied by a reduced production of IgE antibodies, reduced eosinophilia and impaired production of the IL-5, IL-10 and TNF- α cytokines. *In vitro*, *K. pinnata* prevented antigen-induced mast cell degranulation and histamine release [16].

5.5 Antileishmanial Activity

The effect of a leaf extract of *K. pinnata* in mice infected with *Leishmania amazonensis* was investigated. Oral treatment with aqueous leaf extract of *K. pinnata* daily, prevented lesion growth and decreased number of living parasites compared to reference drug, Glucantime. The oral route had showed higher activity compared to other routes [38]. Quercitrin, one of the constituents of the biologically active aqueous extract obtained from *K. pinnata* is demonstrated to be potent antileishmanial compound with a low toxicity profile. This was the first time that antileishmanial activity is demonstrated for a flavonoid glycoside. Also, they identified three flavonoids from the aqueous leaf extract of *K. pinnata* and those were tested separately against *Leishmania* in comparison with standard flavonoids quercitrin, quercetin and afzelin. Among the important structure activity relationship findings is the role of quercetin aglycone and rhamnosyl unit linked at C-3 [22, 39]. Lately they indicated that quercetin glycosides are important active components of the aqueous extract and that they possess potent oral efficacy against cutaneous leishmaniasis [40].

5.6 CNS depressant Activity

The methanol fraction of *Bryophyllum pinnatum* leaf extract had produced alteration of behavior pattern, caused dose-dependent potentiation of pentobarbitone sleeping time and had significant analgesic activity. On the other side reduction of exploratory behavior and loss of residual curiosity were observed [41].

5.7 Anti-inflammatory Activity

Kalanchoe brasiliensis leaf extracts were obtained before and during the blooming season and then tested for the anti-inflammatory effect on carrageenin-induced rat paw oedema; the leaf extract obtained before blooming showed an inhibitory effect on paw oedema induced by carrageenin while extract obtained during blooming showed no inhibitory effect [9]. Further tests were done to investigate the anti-inflammatory effect of juice obtained from leaves of *K. brasiliensis* on zymosan-induced inflammation. Mice received a subcutaneous injection of zymosan in the footpad. Beginning 2 days after the injection, mice were treated daily for 5

days with different concentrations of lyophilized *K. brasiliensis* juice dissolved in water. Treatment had shown reduced footpad thickness, leukocyte infiltration and blood flow in the footpad area. Popliteal lymph node weight in zymosan-injected mice had also decreased, in comparison with indomethacin [42]. The anti-inflammatory activity of the fresh juice was attributed to the presence of kalanchosine dimalate (KMC), an anti-inflammatory salt [34].

5.8 Thyroid peroxidase inhibitor Activity

The *Kalanchoe brasiliensis* aqueous extract is able to scavenge H₂O₂ *in vitro* which is an essential thyroid peroxidase (TPO) cofactor. *Kalanchoe brasiliensis* may be responsible for the inhibition of the iodide-oxidation reaction catalyzed by this enzyme by trapping of hydrogen peroxide. Thus, the chronic uptake of the *K. brasiliensis* aqueous extract may lead to the development of goiter and hypothyroidism [43].

5.9 Cytotoxic Activity

The cytotoxic activity of different *Kalanchoe* species was investigated and tested either for the whole plant extract or the isolated compounds. Bryophyllin B, a potent cytotoxic bufadienolide were isolated from *Bryophyllum pinnatum* and tested against various tumor cells [29]. Five bufadienolides from the leaves of *K. pinnata* and *K. daigremontiana* × *tubiflora* had showed potential cancer chemopreventive activity [44]. The aerial parts of *K. gracilis* had shown cytotoxic activity of against a panel of human tumor cell lines, with potency reaching the nanomolar range. However, few compounds had inhibited HIV replication in H9 lymphocyte cells [31]. The methanol extract of *K. hybrida* towards showed significant cytotoxicity toward MCF-7 (Breast carcinoma cell line) and NCI-H460 (large cell carcinoma of lung cell line) at the tested concentration [12]. The aqueous and the alcoholic extracts of the leaves of *K. thrysiflora* and *K. marmorata* and their fractions (methylene chloride, ethyl acetate and n-butanol) were evaluated for their cytotoxic activity against MCF7 (Breast carcinoma cell line). From the most active cytotoxic fraction, methylene chloride, the cytotoxicity of the isolated compounds were evaluated against normal (HFB4) and cancer (MCF7) cells. 3-oxo-olean-12-ene and β -sitosterol showed similar cytotoxic activity on MCF7 but they were more selective on the cancer cells and not the normal cells HFB4 [33].

5.10 Hepatoprotective Activity

The juice of the leaves and the ethanol extract of the marc left after expressing the juice of *K. pinnata* in rats were tested in CCl₄-induced hepatotoxicity model. The test material was found effective as hepatoprotective as evidenced by *in-vitro*, *in-vivo* and histopathological studies. The juice was found more effective than ethanol extract [45].

5.11 Antioxidant Activity

The aqueous extract of *K. pinnata* was evaluated for its protective effects on gentamicin-induced nephrotoxicity in rats. *In vitro* studies revealed that the *K. pinnata* leaf extract possesses significant antioxidant as well as oxidative radical scavenging activities. The aqueous leaf extract of *K. pinnata* may have a nephroprotective effect in case of gentamicin-induced nephrotoxicity [46].

5.12 Analgesic Activity

The analgesic properties of the aqueous and ethanol extracts of the dry leaves of *K. crenata* were evaluated on the pain induced by acetic acid, formalin and by pain induced by pressure on rats models [47]. While the methylene chloride/methanol (1:1) of *K. crenata* extract and its hexane, methylene chloride, ethyl acetate, *n*-butanol fractions and aqueous residue were also tested using acetic acid, formalin and pressure test models. The methylene chloride/methanol (1:1) extract exhibited a significant analgesic activity other than its fractions [48].

5.13 Anticonvulsant Activity

The anticonvulsant effects of methylene chloride / methanol extract of *K. crenata* was evaluated on seizures induced by pentylenetetrazol, strychnine sulphate and thiosemicarbazide. The extract significantly increased the latency period in seizures induced by pentylenetetrazol and significantly reduced the duration of seizures induced by the three convulsant agents. The extract protected 20% of animals against death in seizures induced by strychnine sulphate and thiosemicarbazide [48].

5.14 Antimicrobial Activity

The 60% methanol extract of *Bryophyllum pinnatum* leaf inhibited the growth of *Bacillus subtilis*, *Escherichia coli*, *Proteus vulgaris*, *Shigella dysenteriae*, *Staphylococcus aureus* while *Klebsiella pneumonia*, *Pseudomonas aeruginosa* and *Candida albicans* were found to resist the action of the test extract [11]. The activity of the hydroalcohol extracts *K. petitiiana*, which was traditionally used in the treatment of various skin disorders, for its antimicrobial activity against different strains of bacteria and fungi was shown to cause different types of skin infections [49]. The antibacterial activity of the methanol extract of *K. farinace* was demonstrated against Gram-positive bacteria including multiresistant *Staphylococcus* strains [50]. Different extracts from the leaves of *Bryophyllum pinnatum* and *K. crenata* were screened for their antimicrobial activities. The leaves were extracted by different solvents viz. water, methanol, local solvents such as palm wine, local gin (Seaman's Schnapps 40% alcoholic drink,) and "omi ekan-ogi" (Sour water from 3 days fermented milled maize). Also one of the methods to prepare an extract was to squeeze raw juice from the leaves. All extracts were lyophilized. Then they were tested against different Gram-negative, Gram-positive organisms and a fungus using Agar well diffusion and broth dilution methods were used to determine the minimum inhibitory concentration (MIC) and minimum bactericidal concentration (MBC); this experiment showed different antimicrobial activities against certain strains [51]. The *n*-hexane, carbon tetrachloride and chloroform soluble fractions of a crude methanol extract of the whole plant of *Bryophyllum daigremontianum* were subjected to antimicrobial activity and brine shrimp lethality bioassay. The carbon tetrachloride soluble partitionate of the methanol extract exhibited significant antimicrobial activity and the most potent cytotoxic activity [52].

5.15 Inhibition of B cell development Activity

A highly purified compound named kalanchosine dimalate (KMC) was obtained from *K. brasiliensis* inhibited of B cell development in the bone marrow, without affecting the myeloid lineage development. *In vitro*, KMC inhibited the interleukin-7 dependent proliferation of B cell precursors and do not induce cell death. Thus results showed that kalanchosine

dimalate can selectively affect B cell lymphopoiesis, possibly acting on the IL-7 signaling pathway, opening new perspectives for a potential therapeutic usage of *K. brasiliensis* derived drugs [53].

5.16 Cardiovascular Effects

The effects of the *n*-butanol extract from the leaves of *K. crenata* was examined on rat blood pressure and guinea pig papillary muscle contraction and action potential. When administered intravenously at different doses, the *n*-butanol extract of *K. crenata* leaves induced a significant transient fall in blood pressure and reduced cardiac rate for about 10 min. Concomitantly, the extract significantly increased the PR, QRS, and QT intervals of the electrocardiogram (ECG). The *n*-butanol extract was found to increase the amplitude of electrical contraction of papillary. When tested on the ventricular myocardial cell action potential, the extract significantly and time dependently delayed the repolarization without affecting the amplitude. The bradycardic effect of the *n*-butanol extract may result from the increase of the PR, QRS, and QT intervals which are in accord with the delay in action potential repolarization observed in *in vitro* studies. The data obtained in the *in vitro* studies suggested that *K. crenata* possess potassium channel blockade properties that may account for its cardiac properties [54].

5.17 Antihyperglycemic Activity

The effect of the water-ethanol extract of *K. crenata* on blood glucose levels was investigated in fasting normal and diet-induced diabetic rats after a short- and medium-term treatment. Diabetes was induced by submitting Wistar rats to a hypercaloric sucrose diet over 4 months. The water-ethanol extract of *K. crenata* exhibited significant increase in the insulin sensitivity index compared with the initial time and to the untreated diabetic animals. Animals treated for 4 weeks exhibited a slight resistance in body-weight gain and decrease in food and water intake comparable with the glibenclamide effects [55].

5.18 Acetylcholinesterase Inhibition Activity

The extracts of *K. brasiliensis*, *K. pinnata* and *K. gastonis-bornieri* showed acetylcholinesterase inhibitory effects and a toxic effect on *Aedes aegypti* larvae [23].

5.19 Insecticidal and Larvicidal Activity

The methanol extract of the leaves of *K. pinnata* [30] and the methanolic extract of the leaves of *K. daigremontiana* and *K. tubiflora* were assessed against the third instar larvae of silkworm (*Bombyx mori*). The results suggest that the orthoester and α -pyrone moieties of bryophyllin A, bryophyllin B, daigromontianin played an important role in this activity [15]. The extracts of *K. brasiliensis*, *K. pinnata* and *K. gastonis-bornieri* showed a toxic effect on *Aedes aegypti* larvae [23].

5. TOXICITY OF KALANCHOE

The bufadienolides found in *Bryophyllum* (*Kalanchoe*) species are toxic to cattle and other farm stocks. *Bryophyllum* poisoning causes anorexia, depression, ruminal atony, diarrhea, heart rate, rhythm abnormalities, dyspnea and death. Myocardial degeneration and necrosis with hemorrhages of the heart and the alimentary tract have been also observed [6].

6. DNA PROFILING

A comparative DNA profiling of samples of fresh leaves of both *K. thyrsiflora* and *K. marmorata* leaves were established. A 67.66% polymorphism was attained using ten different primers with the most relevant primer used for discrimination being OPB-09 and OPA-11 RAPD primers [33].

7. CONCLUSION

There is an increasing interest worldwide for herbal medicine specially those which had been used in traditional folklore medicine. Lately, deep pharmacological assays had been done to investigate the reason for the biological activities of these plants to correlate their use with their phytoconstituents. This literature survey revealed that genus *Kalanchoe* had been thoroughly used in traditional medicine in different areas along the world. Also, genus *Kalanchoe* contains many bioactive constituents as polysaccharides, flavonoids, sterols, organic acids, triterpenoids, phenolic components and bufadenolides. All these phytoconstituents proved to possess different biological activities viz. antimicrobial, analgesic, anti-inflammatory, antiviral, sedative, antiulcer, immunomodulatory, antileishmanial, CNS depressant, thyroid peroxidase inhibitor, cytotoxic activity, hepatoprotective, inhibition of B cell development, cardiovascular effects, antihyperglycemic, acetylcholinesterase inhibitory, and insecticidal. We are confident that further studies may be needed to declare more phytoconstituents and biological activities. Also clinical trials had not been recorded up till now so we would like to suggest that researchers all over the world may invade this untouchable area of research.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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