Kalanchoe brasiliensis Camb. and *Kalanchoe pinnata* (Lamk.) Pers.

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Kalanchoe pinnata (Lamk.) Pers
Photo: Source: data bank from Laboratório de Ecologia e Evolução de sistemas socioecológicos

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Abstract *Kalanchoe brasiliensis* Cambs. and *Kalanchoe pinnata* (Lamk.) Pers species belong to *Crassulaceae* family. *Kalanchoe brasiliensis* is popularly known as '*saião'*, 'white coirama', 'thick leaf', 'leaf of luck' and 'leaf of the coast', and *Kalanchoe pinnata* as '*saião-roxo'*, 'leaf-of-fortune', 'leaf of the coast', 'yellow flower of fortune' and '*para-tudo'*. In ethnopharmacology, there are reports of the use of the extract of the leaves of *Kalanchoe brasiliensis* for skin infections and oral mucosa, bronchitis, nasal congestion, chest infections, yellow fever, gastric ulcers and arthritis. Leaves and stalks are the most commonly used parts. The leaves of *K. brasiliensis* contain high concentrations of flavonoids; while fatty acids, acyclic and aromatic organic acids, amino acids, bufadienolides, α-β unsaturated acyclic ketones, fenantrenic derivatives, sterols, long-chain hydrocarbons and triterpenoids are found mainly in the leaves of *K. pinnata*. Analgesic, anti-inflammatory, anti-leishmaniotic, antimalarial, antipyretic, antimicrobial, antithyroidal, antitumor, antiulcer, hepatoprotective, immunosuppressive, pesticide, inhibition in uterine contractions, neuropsicofarmacologic and hypoglycemic properties of these species have already been evaluated in experimental pharmacology.

Keywords Saião · Flavonoids · *Kalanchoe* · *Crassulaceae*

1 Taxonomic Characteristics

Kalanchoe pinnata and *Kalanchoe brasiliensis* belong to the genus *Kalanchoe* (synonym *Bryophyllum* and *Cotyledon*), family *Crassulaceae* (Maurice 1993). Popular names include plant of life, air plant, plant of love, canterbury bells, cathedral bells, green love, curtain plant, parnabija, white coirama, coirama-brava, leaf of the coast and *saião* (Anjoo and Kumar 2000).

Synonyms Both species have botanical synonyms: *Kalanchoe brasiliensis* syn *Cotyledon brasilica* Vell, *Kalanchoe pinnata* syn *Bryophyllum pinnatum* (Lamk.) Oken; *Bryophyllum pinnatum* Kurz., *Cotyledon pinnata* Lamk, among others.

2 Crude Drug Used

The aqueous extract of the leaves of *K. pinnata* has been used for the treatment of cutaneous leishmaniasis and to decrease acute anaphylactic reactions (Cruz et al. 2008, 2012). Investigating anti-tumor action of *Kalanchoe brasiliensis*, an aqueous solution containing 50 mg/kg of the raw extract diluted in saline was administered intraperitoneally in mice, showing that it could be used for treatment of sarcoma 180 (Machado and Melo-Junior 2009).

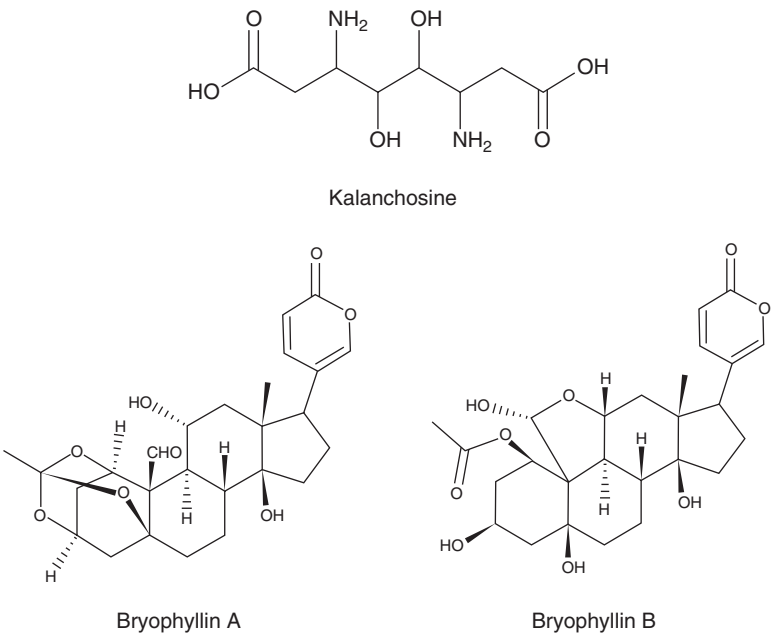

Fig. 1 Chemical structures of the main compounds isolated from *Kalanchoe*. (**a**) Kalanchosine (1), 3,6-diamino-4,5-dihydroxyoctanedioic acid and (**b**) Bryophillin A and B

3 Major Chemical Constituents and Bioactive Compounds

Species of the genus *Kalanchoe* contain a wide variety of secondary substances, mainly terpenes (Anjoo and Kumar 2000; Siddiqui et al. 1989), flavonoids (Gaind and Gupta 1972; Muzitano et al. 2006), alkaloids (Biswas 2011; Okwu and Josiah 2006), bufadienolides (Anjoo and Kumar 2000; Milad et al. 2014; Supratman et al. 2001) glycosides, steroids, saponins, tannins, reduced sugars and aminoacids (Biswas 2011; Matthew et al. 2013; Pattewar 2012) (Fig. 1).

Flavonoid glycosides derived from patuletin were isolated from the leaves and branches of *K. brasiliensis*, as 8-methoxykaempferol-3,7-di-O- rhamnopyranoside, as 8-methoxyquercetin, 3,7-di-O-rhamnopyranoside and quercetin (Trevisan et al. 2006; Veiga-Junior 2005). Malic acid and an organic salt – kalanchosin dimalate (KMC), belonging to a new class of metabolites, called kalanchosine – were isolated from extracts of areal parts of *K. brasiliensis* (Costa et al. 2006).

From *K. pinnata*, triterpenes and sterols were identified such as α and β-amyrin, taraxerol, acetylated derivatives of cycloartan-3-ol, ψ-taraxasterol; (24R) – stigmast-5, 25-dien-3β-ol (24 epiclerosterol); (24R) – 5α- stigmast-7, 25-dien-3β-ol; 5α- stigmast- 24-en-3β-ol; 25 methyl-5α-ergost-24 (28) – en-3β-ol, and others. The bufadienolides isolated from *K. pinnata* were identified as bryophillin A and B (Supratman et al. 2001). The presence of bufadienolids suggests a potential antitumor and bactericidal ability (Pattewar 2012; Supratman et al. 2001).

The compounds α-ramnoisorobin, kaempferitrine (Tatsimo et al. 2012) and quercetin (Muzitano et al. 2006) are among flavonoids isolated from *K. pinnata*. Due to the restricted occurrence and great abundance of flavonoids in *K. pinnata*, it has been suggested that this class of metabolites may be responsible for the high therapeutic potential of the species (Pattewar 2012).

4 Morphological Description

K. brasiliensis has herbaceous features and grows to a height of 30 cm to 1 m. Leaves are sparsely branched, oval or obovate oppositely succulent, peciolated and crenated. A characteristic feature that facilitates differentiation between *K. pinnata* and *K. brasiliensis* species is the appearance of the leaf, since the latter has a corrugated subcrenated edge, whereas *K. pinnata* has a crenated leaf. *K. brasiliensis* has a yellow-orange inflorescence with small flowers (Lorenzi and Matos 2008).

5 Geographical Distribution

The *Kalanchoe* genus includes native species from Africa and Brazil (Boulos 1999). In Brazil, *K. brasiliensis* is a native species, with an area from the southeast to the northeast. It is common in the coastal zone. *K. pinnata* has a pantropical distribution, both continental and insular (Veiga-Junior 2005).

6 Ecological Requirements

Species of the genus *Kalanchoe* inhabit different regions, ranging from rainforests to arid environments (Rauh 1973).

K. pinnata is intolerant to long periods of drought. As invasive species, it adapts and colonizes different areas, are abundant in sandy soils and rocky coastal regions in different countries, such as Madagascar, the United States, Brazil and Australia. It is still found in areas with human disturbance. It adapts to humid and semi-humid climates, with a precipitation between 1000 and 2000 mm (Smith 1985).

7 Collection Practice

The special literature relating to the harvesting of *K. pinnata* and *K. brasiliensis* is either scarce or unavailable. In general, during collection of medicinal plants, one should take into account population survival and maintenance of the ecosystem.

Furthermore, the species should be collected during the appropriate season, climate and time, as the secondary metabolites are variable according to different periods (World Health Organization 2003).

8 Traditional Use and Common Knowledge

Different species of the genus *Kalanchoe* are traditionally used in folk medicine in many parts of the world, particularly in South America. In Guyana, the leaves of *K. pinnata* are traditionally used as an anti-inflammatory and antiseptic to treat coughs, ulcers and wounds (El Abdellaoui et al. 2010). In Brazil, the most studied and used species are *K. pinnata* and *K. brasiliensis*.

K. brasiliensis is widely used in the treatment of boils. The pure juice is used orally in cases of ovarian and uterine inflammation or mixed with other plants such as *malvarisco*, used in the preparation of cough syrups. *K. pinnata* is used in inflammatory diseases, gastric ulcers, burns, diarrhea, vomiting, insect bites, body aches, and as an antifungal and antibacterial (Almeida et al. 2000; Anjoo and Kumar 2000; Okwu and Josiah 2006).

9 Modern Medicine Based on Uses Its Traditional Medicine

K. brasiliensis and *K. pinnata* are extensively used in traditional medicine. There are a significant number of studies that describe their biological effects, especially for *K. pinnata*. However, the evaluation of the active chemical compounds and their biological activity is far from being complete. There is also a need for more detailed studies looking on large scale production and economic viability. Preclinical studies of pharmacological activities in vitro and in vivo are also described in the special literature on these species.

In vitro assays using extracts of the leaves of different species of the genus Kalanchoe (including *K. brasiliensis*) in ethyl acetate, hexane and methanol acetate, identified larvicidal activity effective against *Aedes aegypti* at concentrations of 500, 250 and 100 ppm (Salles Trevisan et al. 2006). Two bufadienolids isolated from *K. pinnata* demonstrated a high degree of effectiveness against the third larval stage of the silkworm (Supratman et al. 2001).

In vitro assays showed that the raw extract of *Kalanchoe brasiliensis* contains active substances with antitumor effects against Sarcoma 180 cells. The results indicated an inhibitory effect of the growth of this kind of tumor, with 52.8% reduction ($p < 0.05$) of tumor mass (Machado and Melo-Junior 2009). Raw extract and fractions of *K. pinnata* also exhibited dose-dependent cytotoxic activity, with IC_{50} 550.0 μg/mL and 91.0 μg/mL, respectively; against cervical cancer (Mahata et al. 2012). Additionally, it exhibited cytotoxic activity against KB cells (Yamagishi et al. 1989). Finally, leaves of the species have been shown to have anti-mutagenic properties (Obaseiki-Ebor et al. 1993).

The leaf extract of *Kalanchoe pinnata* in dichloromethane (DCM), chloroform, petroleum ether and aqueous fractions have been evaluated in an oral glucose tolerance test (OGTT) at a concentration of 10 mg/kg in rats. In this study, the fraction in DCM produced an improved hypoglycemic action. In addition, the dose-dependent effects of the same fraction of *Kalanchoe pinnata* were evaluated. It was concluded that the DCM fraction demonstrated antihyperglycemic activity in a dose-dependent pattern, which is comparable to the glibenclamide (with the same dose of 2.5 mg/kg body weight). According to researchers, among four concentrations tested, the maximum concentration used (10 mg/kg body weight) showed prominent hypoglycemic activity (Patil et al. 2013). The study by Ojewole (2005) demonstrated significant hypoglycemia in mice when treated with aqueous extract of *K. pinnata*.

In models of severe anaphylactic reaction, the aqueous extract of leaves of *Kalanchoe pinnata* was effective. In studies by Cruz et al. (2012) the effect of *K. pinnata* flavonoids quercetin (QE) and quercitrin (IQ) was evaluated in the activation of mast cells in vitro in a model of the allergic disease in vivo. The study showed that this extract and QE prevented mast cell degranulation and lessened the action of TNF and IL-6 released in vitro and in vivo. These findings demonstrate that treatment with *K. pinnata* or QE is effective in the treatment of allergic respiratory diseases, providing new perspectives on the immunomodulatory functions of this plant.

The leaf extract of *K. pinnata* in DCM/methanol (1:1) and hexane/DCM reduced at least 30% acetic acid-induced pain and also increased the latency period between seizures (Nguelefack et al. 2006). The effect was greater with higher doses per kilogram (between 200 and 300 mg/kg) (Veiga-Junior 2005).

Cruz et al. (2008) identified a protective effect of aqueous extract of *K. pinnata* in fatal anaphylactic shock, an immune-mediated Th2 pathology, and also identified the active component. Mice oral treated daily with the extract survived during sensitization with ovalbumin when tested with this allergen, while there was a 100% mortality rate in the untreated group. The intraperitoneal single dose 3 h before the test was partially effective. Oral protection was accompanied by a decreased production of anti-OVA IgE antibodies, eosinophilia and decreased the production of cytokines IL-5, IL-10 and TNF-α. In vitro, these extract prevented mast cell degranulation and histamine release induced by antigens. Oral treatment with the flavonoid quercitrin from *K. pinnata* prevented fatal anaphylaxis in 75% of animals. These results indicate that oral treatment effectively attenuates anaphylactic pro-immune responses. The protection obtained with quercitrin, although not maximal, suggests that the flavonoid is a critical component of *K. pinnata* extract against this extreme allergic reaction.

Studies by Biswas et al. (2011) evaluated ethanol extracts of leaves and stems of *K. pinnata*. The ethanolic extract demonstrated significant antimicrobial activity against gram-positive (*B. subtilis, S. aureus*) and gram-negative (*E. coli, P. aeruginosa, S. dysenteriae*) bacteria, with zones of inhibition of 6.0 ± 0.35 to 8.2 ± 0.22 mm.

Yadav and Dixit (2003) observed that the juice of the fresh leaves of *K. pinnata* was used as a treatment for jaundice, and the ethanolic extract was tested on rats

against tetrachloride-induced hepatotoxicity. The test was effective in vivo and in vitro, based on the histological analysis. The juice was more effective than the ethanol extract. In another study using the aqueous extract in mice, showed that this extract protect the gentamicin-induced nephrotoxicity. A significant antioxidant activity of the aqueous extract was observed in the same study (Harlalka et al. 2007).

There was a reduction in blood pressure in rats after administration of the aqueous leaf extract of *K. pinnata*. In rabbits, this extract protected the kidneys and the liver (Ghasi et al. 2011). The alcoholic extract of the leaves administered orally and intraperitoneally in rats showed significant diuretic action, especially with the intraperitoneal administration (Patil et al. 2013).

According to tests in a murine model of cutaneous leishmaniasis, where different flavonoids were used, the glycosides were defined as active compounds with evident action against *Leishmania amazonensis* (Muzitano et al. 2006).

10 Conclusions

The widespread use of the genus *Kalanchoe*, and specifically of the species *K. brasiliensis* and *K. pinata* in traditional medicine, as well as their acceptance by many researchers, is strong evidence that these species can be effective for treating the conditions described and can be considered as a possible source for healing the pathological cases investigated. Extracts of *K. pinnata* and *K. brasiliensis* have been reported to possess anti-inflammatory, antihypertensive, antimicrobial, antifungal, antidiabetic and antitumor effects. Several active compounds have been identified in *K. pinnata,* such as glycosides, organic acids, steroids and bufadienolides. These compounds have also a variety of demonstrated effects including antibacterial and antitumor effects.

References

Almeida AP, Da Silva SAG, Souza MLM, Lima LMTR, Rossi-Bergmann B, Gonçalves de Moraes VL, Costa SS (2000) Isolation chemicals analysis of a fatty acid fraction of *Kalanchoe pinnata* with a potent lymphocyte suppressive activity. Planta Med 66:134–137

Anjoo K, Kumar SA (2000) Microscopical and preliminary phytochemical studies on aerial part (leaves and stem) of *Bryophyllum pinnotum* Kurz. Pharm J 2:254–259. https://doi.org/10.1016/S0975-3575(10)80113-0

Biswas K (2011) Literature review on pharmacological potentials of *Kalanchoe pinnata* (Crassulaceae). Afr J Pharm Pharmacol 5:1258–1262. https://doi.org/10.5897/AJPP11.273

Biswas SK, Chowdhury A, Das J, Karmakar UK, Shill MC (2011) Assessment of cytotoxicity and antibacterial activities of ethanolic extracts of *Kalanchoe pinnata linn.* (family: crassulaceae) leaves and stems. Int J Pharm Sci Res 2:2605–2609

Boulos L (1999) Flora of Egypt. Vol. 1 (Azollaceae – Oxalidaceae), nordic. J Bot 19(3):328. https://doi.org/10.1111/j.1756-1051.1999.tb01119.x

Costa SS, de Souza MDLM, Ibrahim T, de Melo GO, de Almeida AP, Guette C, Férézou J-P, Koatz VLG (2006) Kalanchosine dimalate, an anti-inflammatory salt from *Kalanchoe brasiliensis*. J Nat Prod 69:815–818. https://doi.org/10.1021/np050475+

Cruz E, Da-Silva S, Muzitano MF, Silva PMR, Costa SS, Rossi-Bergmann B (2008) Immunomodulatory pretreatment with *Kalanchoe pinnata* extract and its quercitrin flavonoid effectively protects mice against fatal anaphylactic shock. Int Immunopharmacol 8:1616–1621. https://doi.org/10.1016/j.intimp.2008.07.006

Cruz E, Reuter S, Martin H, Dehzad N, Muzitano MF, Costa SS, Rossi-Bergmann B, Buhl R, Stassen M, Taube C (2012) *Kalanchoe pinnata* inhibits mast cell activation and prevents allergic airway disease. Phytomedicine 19:115–121. https://doi.org/10.1016/j.phymed.2011.06.030

El Abdellaoui S, Destandau E, Toribio A, Elfakir C, Lafosse M, Renimel I, André P, Cancellieri P, Landemarre L (2010) Bioactive molecules in *Kalanchoe pinnata* leaves: extraction, purification, and identification. Anal Bioanal Chem 398:1329–1338. https://doi.org/10.1007/s00216-010-4047-3

Gaind KN, Gupta RL (1972) Alkanes, alkanols, triterpenes and sterols of *Kalanchoe pinnata*. Phytochemistry 11:1500–1502. https://doi.org/10.1016/S0031-9422(00)90117-1

Ghasi S, Egwuibe C, Achukwu PU, Onyeanusi JC (2011) Assessment of the medical benefit in the folkloric use of *Bryophyllum pinnatum* leaf among the igbos of Nigeria for the treatment of hypertension. Afr J Pharm Pharmacol 5:83–92. https://doi.org/10.5897/AJPP10.309

Harlalka GV, Patil CR, Patil MR (2007) Protective effect of *Kalanchoe pinnata* pers. (Crassulaceae) on gentamicin-induced nephrotoxicity in rats. Indian J Pharmacol 39(4):201–205. https://doi.org/10.4103/0253-7613.36540

Lorenzi H, Matos FJA (2008) Plantas Medicinais no Brasil – Nativas e Exóticas, 2nd edn. Instituto Plantarum, Nova Odessa

Machado MCF, Melo-Junior MR (2009) Evaluation of antitumoral effect of the *Kalanchoe brasiliensis* on the Sarcoma 180 on rats. Rev Eletrônica Farmácia VI:1–6

Mahata S, Maru S, Shukla S, Pandey A, Mugesh G, Das BC, Bharti AC (2012) Anticancer property of *Bryophyllum pinnata* (Lam.) Oken. leaf on human cervical cancer cells. BMC Complement Altern Med 12:15–15. https://doi.org/10.1186/1472-6882-12-15

Matthew S, Jain AK, James M, Matthew C, Bhowmik D (2013) Analgesic and anti-inflammatory activity of *Kalanchoe pinnata* (Lam.) Pers material. J Med Plants Stud Analg 1:23–28

Maurice M (1993) Handbook of African medicinal plant. CRC Press, London

Milad R, El-Ahmady S, Singab AN (2014) Genus *Kalanchoe* (Crassulaceae): a review of its ethnomedicinal, botanical, chemical and pharmacological properties. Eur J Med Plants 4(1):86–104

Muzitano MF, Cruz EA, De Almeida AP, Da Silva SAG, Kaiser CR, Guette C, Rossi-Bergmann B, Costa SS (2006) Quercitrin: an antileishmanial flavonoid glycoside from Kalanchoe pinnata. Planta Med 72:81–83. https://doi.org/10.1055/s-2005-873183

Nguelefack TB, Nana P, Atsamo AD, Dimo T, Watcho P, Dongmo AB, Tapondjou LA, Njamen D, Wansi SL, Kamanyi A (2006) Analgesic and anticonvulsant effects of extracts from the leaves of Kalanchoe crenata (Andrews) Haworth (Crassulaceae). J Ethnopharmacol 106:70–75. https://doi.org/10.1016/j.jep.2005.12.003

Obaseiki-Ebor EE, Odukoya K, Telikepalli H, Mitscher LA, Shankel DM (1993) Antimutagenic activity of extracts of leaves of four common edible vegetable plants in Nigeria (West Africa). Mutat Res Lett 302:109–117. https://doi.org/10.1016/0165-7992(93)90012-K

Ojewole JAO (2005) Antinociceptive, anti-inflammatory and antidiabetic effects of *Bryophyllum pinnatum* (Crassulaceae) leaf aqueous extract. J Ethnopharmacol 99:13–19. https://doi.org/10.1016/j.jep.2005.01.025

Okwu DE, Josiah C (2006) Evaluation of the chemical composition of two Nigerian medicinal plants. Afr J Biotechnol 5:357–361

Patil S, Dongare V, Kulkarni C, Joglekar M, Arvindekar A (2013) Antidiabetic activity of Kalanchoe pinnata in streptozotocin-induced diabetic rats by glucose independent insulin secretagogue action. Pharm Biol 51:1411–1418. https://doi.org/10.3109/13880209

Pattewar SV (2012) *Kalanchoe pinnata*: phytochemical and pharmacological profile. Int J Phytopharm 1:1–8. https://doi.org/10.7439/ijpp.v2i1.223

Rauh W (1973) Über die Zonierung und Differenzierung der Vegetation Madagaskars. Akad Wiss Mainz. Trop Subtrop Pflanzenwelt 1:146

Salles Trevisan MT, Barbosa Bezerra MZ, Pinheiro Santiago GM, Feitosa CM, Verpoorte R, Braz Filho R (2006) Atividades larvicida e anticolinesterésica de plantas do gênero *Kalanchoe*. Quim Nova 29:415–418. https://doi.org/10.1590/S0100-40422006000300002

Siddiqui S, Faizi S, Siddiqui BS, Sultana N (1989) Triterpenoids and phenanthrenes from leaves of *Bryophyllum pinnatum*. Phytochemistry 28:2433–2438. https://doi.org/10.1016/S0031-9422(00)97999-8

Smith AC (1985) Flora Vitiensis nova: a new flora of Fiji. Natl Trop Bot Gard Lawai 3:624–625. https://doi.org/10.5962/bhl.title.44033

Supratman U, Fujita T, Akiyama K, Hayashi H, Murakami A, Sakai H, Koshimizu K, Ohigashi H (2001) Anti-tumor promoting activity of bufadienolides from *Kalanchoe pinnata* and *K. daigremontiana x tubiflora*. Biosci Biotechnol Biochem 65:947–949. https://doi.org/10.1271/bbb.65.947

Tatsimo S, Tamokou J, Havyarimana L, Csupor D, Forgo P, Hohmann J, Kuiate J-R, Tane P (2012) Antimicrobial and antioxidant activity of kaempferol rhamnoside derivatives from *Bryophyllum pinnatum*. BMC Res Notes 5:158. https://doi.org/10.1186/1756-0500-5-158

Trevisan MTS, Zeneide M, Bezerra B, Maria G, Santiago P (2006) Atividades larvicida e anticolinesterásica de plantas do gênero *Kalanchoe*. Quim Nova 29:415–418

Veiga-Junior VF (2005) *Kalanchoe brasiliensis* Camb. *Kalanchoe pinnata* (Lamk.), In: Amaral A (Org.), Coletânea científica de plantas de uso medicinal. Editora FioCruz, Rio de Janeiro

World Health Organization (2003) WHO guidelines on good agricultural and collection practices (GACP) for medicinal plants. World Health 99:67–73

Yadav NP, Dixit VK (2003) Hepatoprotective activity of leaves of *Kalanchoe pinnata* Pers. J Ethnopharmacol 86:197–202. https://doi.org/10.1016/S0378-8741(03)00074-6

Yamagishi T, Haruna M, Yan X-Z, Chang J-J, Lee K-H (1989) Antitumor agents, 110, bryophyllin B, a novel potent cytotoxic bufadienolide from *Bryophyllum pinnatum*. J Nat Prod 52:1071–1079. https://doi.org/10.1021/np50065a025