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Review

Kalanchoe daigremontiana from Ornamental to Pharmaceutical Applications

Cecilia Guadalupe de Loza-García [1], Ana Belem Rubio-García [1], Salvador Hernández-Estrada [1], Luis Alfonso Hernández-Villaseñor [1], Luis Antonio Ramirez-Contreras [1], Jorge Manuel Silva-Jara [2], Jorge L. Mejía-Méndez [3], Zuamí Villagrán [1], Eugenio Sánchez-Arreola [4], Napoleón González-Silva [1] and Luis Miguel Anaya-Esparza [5,*]

1 Centro Universitario de Los Altos, Universidad de Guadalajara, Tepatitlan de Morelos 47620, Mexico
2 Centro Universitario de Ciencias Exactas e Ingenierías, Universidad de Guadalajara, Guadalajara 44430, Mexico
3 Tecnológico de Monterrey, Escuela de Ingeniería y Ciencias, Epigmenio González 500, San Pablo, Santiago de Querétaro 76130, Mexico
4 Departamento de Ciencias Químico-Biológicas, Universidad de las Américas Puebla, Santa Catarina Mártir s/n, San Andrés Cholula 72810, Mexico
5 Centro de Estudios para la Agricultura, la Alimentación y la Crisis Climática, Centro Universitario de los Altos, Universidad de Guadalajara, Tepatitlán de Morelos 47620, Mexico
* Correspondence: luis.aesparza@academicos.udg.mx

Abstract

Kalanchoe daigremontiana, a succulent herbaceous plant in the Crassulaceae family from Madagascar, has gained global popularity as an ornamental and medicinal species. This review examines the traditional uses, phytochemical composition, biological properties, toxicological aspects, and regulatory challenges of *K. daigremontiana*. The traditional medicinal uses of its leaves and roots include treating burns, rheumatic disorders, hypertension, diabetes, kidney pain, diarrhea, cough, fever, gastric issues, anxiety, inflammation, and cancer. Chemical compounds identified include phenolic acids, flavonoids, tannins, alkaloids, glycosides, saponins, sterols, terpenes, and fatty acids, with phenolic compounds and bufadienolides being predominant. In vitro studies of the crude extracts, bufadienolide-rich fractions, and isolated compounds have shown antioxidant, antibacterial, antifungal, antiviral, antiparasitic, anthelmintic, anti-inflammatory, anticoagulant, anti-aging, cytotoxic, antitumoral, and antiproliferative properties. In vivo studies have demonstrated hepatoprotective, skincare, and cardiac-glycoside-like effects. While crude extracts and bufadienolide-rich fractions have shown toxic effects in 2-week-old chicks, guinea pigs, and *Artemia salina*, no toxicity has been reported in goats, broiler chickens, laying hens, or human erythrocytes. Although *K. daigremontiana*-based products are commercially available as dietary supplements with various health claims, these lack scientific validation. Despite the potential pharmaceutical applications of *K. daigremontiana*, further research is needed to determine its effects, dosage, mechanisms, long-term safety, and side effects, with clinical studies essential to validate its therapeutic potential.

Keywords: medicinal plants; natural products; phytochemicals; pharmacobotanical; cytotoxicity; antimicrobials; antioxidants; health

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1. Introduction

Botanical sources remain indispensable in both traditional and contemporary medicine, serving as abundant reservoirs for the discovery of novel bioactive compounds. Historically, plant-derived secondary metabolites have formed the basis of numerous clinically

approved drugs with diverse therapeutic properties [1,2]. A particularly promising botanical source of therapeutic agents is the Crassulaceae family, notably species in the genus *Kalanchoe* [3–5]. In this context, some members of this genus (*K. pinnata*, *K. laciniata*, and *K. crenata*, and *K. daigremontiana*) possess a longstanding history of therapeutic use and are colloquially referred to as "miracle leaf" due to their remarkable healing properties and traditional applications in treating skin injuries, pain, fever, headache, convulsions, antiseptic needs, burns, arthritis, gastric and menstrual disorders, cough, anxiety, and cancer among others [1,5].

K. daigremontiana, commonly known as the "mother of thousands," is a native of Madagascar and South Africa but has spread to various tropical and subtropical regions worldwide (i.e., Mexico, Brazil, Peru, Australia, India, and Poland). This succulent has gained international recognition not only for its unique asexual reproductive strategy, involving foliar plantlets, but also for its exceptional ecological adaptability. In Mexico, it is primarily used as an ornamental plant due to its aesthetic appeal [6]; however, in some areas, *K. daigremontiana* is considered invasive and toxic [7,8]. Despite these concerns, *K. daigremontiana* has been integrated into traditional medicinal systems across diverse countries worldwide, such as Mexico, the USA, Brazil, Peru, South Africa, India, and Poland [5,8]. Ethnobotanical records document its varied therapeutic applications, ranging from treating inflammatory conditions and microbial infections to its use as a topical cicatrizing agent for wound healing [6,9–15].

The scientific evidence demonstrated that extracts from roots, stems, and leaves of *K. daigremontiana* exhibited antimicrobial, antioxidant, anti-inflammatory, cytotoxic, antitumor, antiproliferative, antidiabetic, antiaging, anticoagulant, and anthelmintic properties [8,11,14,16,17], supporting their recognition as a medicinal plant [18]. According to the literature, most of the biological activities reported on extracts and fractions are attributed to the presence of bioactive compounds, including phenolic acids, flavonoids, alkaloids, saponins, and steroids [1,17]. In this context, *K. daigremontiana* is a significant botanical material of pharmaceutical interest. Therefore, this review aims to synthesize scientific studies that describe the traditional uses, phytochemical constituents, biological properties, toxicological considerations, and regulatory challenges associated with *K. daigremontiana*.

2. Traditional Uses and Health Importance

Kalanchoe daigremontiana is an herbaceous plant commonly cultivated as an ornamental addition to gardens and homes [14]. On the other hand, many people (often from Africa, South and Central America, and Asia) have used this plant species in their traditional healthcare system (i.e., Ayurdeva, Chinese Traditional Medicine, Anthroposophic medicine, and German Homeopathic Pharmacopoeia) [1,19]. In traditional medicine, *K. daigremontiana* leaves or roots are used in infusions, decoctions, cataplasm, crude extracts preparations obtained by maceration, or even compresses from crushed leaves as an alternative treatment for a variety of ailments, such as burns, rheumatic conditions, hypertension, diabetes, kidney pain, diarrhea, infections (antiseptic), cough, fever, deep wounds, gangrene, ulcers, gastric problems, abscesses, anxiety, inflammation, and various types of cancer [9,10,12,14,15,20–23].

Additionally, the extract obtained after crushing fresh leaves from *K. daigremontiana* is used to alleviate skin irritation [13], combat microbial infections, and aid in the treatment of asthma, ulcers, and wound healing [24,25]. Furthermore, in some regions, clean and disinfected *K. daigremontiana* leaves are eaten raw to address leucorrhea and gastric issues [9]. In this context, most bioactivities of *K. daigremontiana* are attributed to the presence of diverse secondary metabolites and bioactive compounds [5,11,19,26,27]. Figure 1 shows the most common preparations for traditional and research uses.

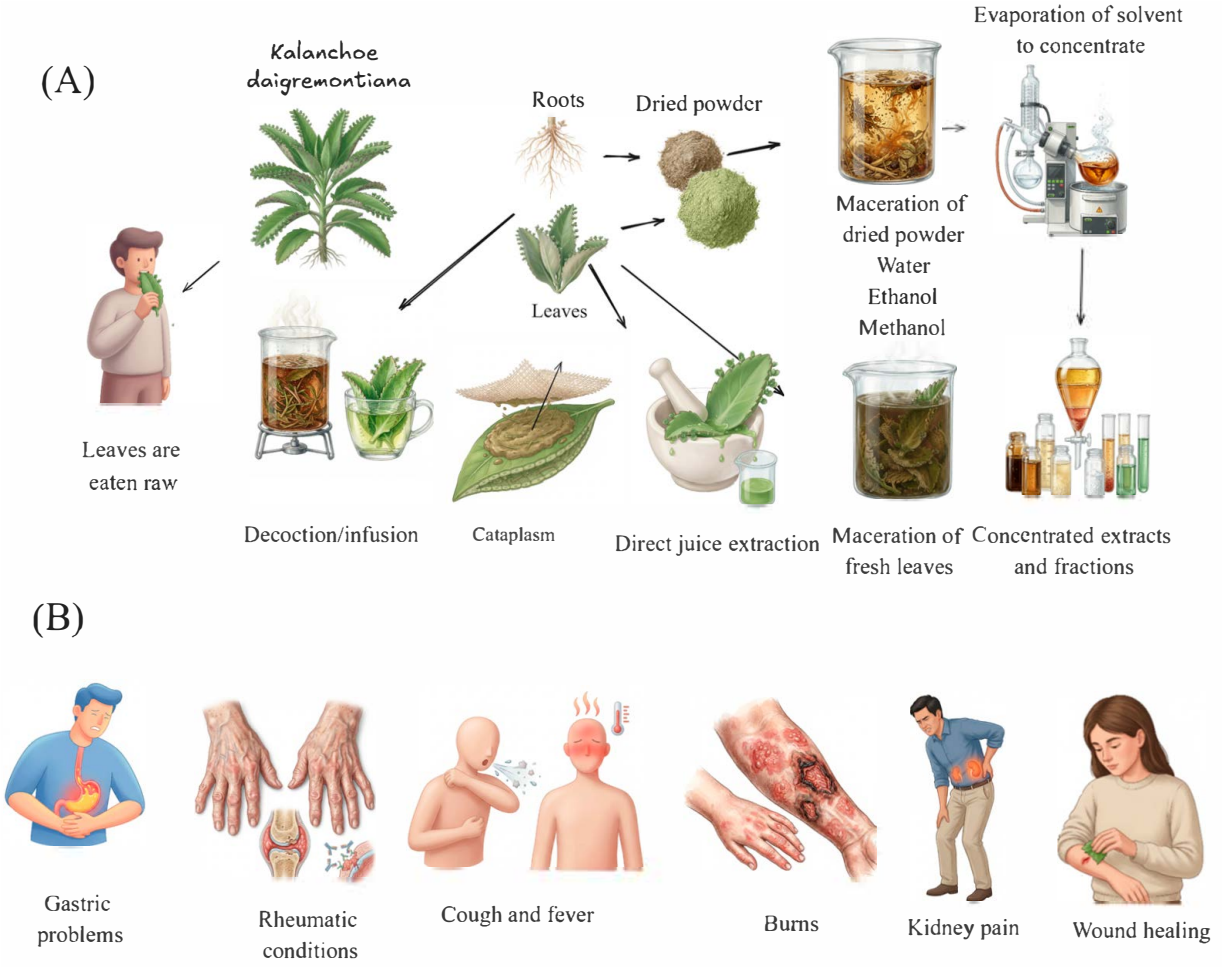


Figure 1. Schematic representation of the most common preparations (**A**) and traditional medicinal uses (**B**) of *Kalanchoe daigremontiana* leaves and roots. Figure created with illustrae.co.

3. Bioactive Compounds Identified in *Kalanchoe daigremontiana*

Phytochemicals are secondary metabolites synthesized by plants that hold potential for the discovery of new pharmaceutical drugs [1,2]. Table 1 lists the various phytochemicals, both qualitative and quantitative, identified in the leaves, roots, flowers, and wax fractions of *K. daigremontiana*, including phenolic acids, flavonoids, tannins, alkaloids, glycosides, saponins, sterols, terpenes, and fatty acids [16,19,28–30]. Among the numerous phytochemicals reported in *K. daigremontiana*, phenolic compounds and bufadienolides are considered the predominant groups. These compounds are responsible for the bioactivity of *K. daigremontiana* [25]. Additionally, qualitative methods for the identification of bioactive compounds include chemical colorimetric reactions (i.e., Folin Ciocalteau's and aluminum chloride reactions) and chromatographic techniques such as Thin-layer chromatography and High-Performance Liquid Chromatography (HPLC), while quantitative methods include HPLC, HPLC with Diode Array Detection (HPLC-DAD), Liquid Chromatography–Electrospray Ionization–Tandem Mass Spectrometry (LC–ESI-MS/MS), Time-of-Flight Mass Spectrometry (TOF-MS), gas chromatography, and nuclear magnetic resonance.

Table 1. Phytochemicals reported in *Kalanchoe daigremontiana*.

Plant Part	Extraction Method	Solvent	Detection/Quantification Method	Reported Compound	Identified/Content	Biological Activity Reported	Ref.
Leaves	Maceration	Methanol	Chemical colorimetric reaction	Sterols Flavonoids Alkaloids Saponins	Identified	Antiparasitic	[16]
Leaves	Accelerated solvent extraction	Ethanol-water (70:30 *v*/*v*)	HPLC-PDA	Total phenolics	14.82 mg/100 g DM	Not reported	[31]
				Total flavonoids	725 mg/100 g DM		
				Total anthocyanins	2.95 mg/100 g DM		
Leaves	Accelerated solvent extraction	Ethanol-water (70:30 *v*/*v*)	LC–ESI-MS/MS	Gallic acid	1.1 µg/g DM	Antioxidant Cytotoxic	[11]
				Chlorogenic acid	0.97 µg/g DM		
				γ-Resorcylic acid	0.21 µg/g DM		
				p-Coumaric acid	1.3 µg/g DM		
				Ferulic acid	72.1 µg/g DM		
				Caffeic acid	16.5 µg/g DM		
				ß-Rosorcylic acid	0.22 µg/g DM		
				Syringic acid	7.46 µg/g DM		
				Protocatechuic acid	24.82 µg/g DM		
Leaves	Maceration with water	Flavonoid-rich fraction	HPLC-DAD NMR spectroscopy	3-O-β-D-xylopyranosyl (1→2) α-L-rhamnopyranoside quercetin-3-O-β-Dxylopyranosyl (1→2) α-L-rhamnopyranoside kaempferol-3-O-β-Dxylopyranosyl (1→2)-α-L-rhamnopyranoside-7-O-β-D-glucopyranoside	Identified	Antiviral Cytotoxic	[32]

Table 1. *Cont.*

Plant Part	Extraction Method	Solvent	Detection/Quantification Method	Reported Compound	Identified/Content	Biological Activity Reported	Ref.
Leaves	Maceration with water	Flavonoid-rich fraction	NMR spectroscopy	kaempferol-3-O-xylopyranosyl(1→2) rhamnopyranoside	Identified	Not reported	[33]
Leaves	Ultrasonic waves	Methanol	TLC/Densitometry	Gallic acid Caffeic acid p-coumaric acid Protocatechuic acid	Identified	Not reported	[20]
Leaves	Percolation	Methanol Ethanol	Mass spectrometry	Aminoacids Tannins Flavonoids Triterpenoids Cardiotonics Alkaloids Leucoanthocyanidin	Identified	Antioxidant	[34]
Leaves	Maceration	Water	UHPLC-DAD-MS	kaempferol 3-O-β-D-xylopyranosyl-(1→2)-α-L-rhamnopyranoside-7-O-β-D-glucopyranoside quercetin 3-O-α-L-arabinopyranosyl-(1→2)-α-L-rhamnopyranoside Daigremontianin isomer Bryophyllin a Kapinnatoside (kaempferol 3-O-α-L-arabinopyranosyl-(1→2)-α-L-rhamnopyranoside) Bersaldegenin-1-acetate Bersaldegenin-2-acetate Daigremontianin Bersaldegenin-1,3,5-orthoacetate	Identified	Antiviral	[35]

Table 1. *Cont.*

Plant Part	Extraction Method	Solvent	Detection/Quantification Method	Reported Compound	Identified/Content	Biological Activity Reported	Ref.
Leaves	Fresh juice after crushing leaves	Not used	Spectrophotometrically	Red carotenoids	0.39 mg/g DM	No information	[19]
				Yellow carotenoids	0.46 mg/g DM		
				Total carotenoids	0.54 mg/g DM		
				Phenolic compounds	21.40 mg/g DM		
				Total flavonoids	17.35 mg/g DM		
Leaves	Maceration	Water	UHPLC-DAD-ESI-MS	Tetrahydroxy-bufadienolide-rhamnoside	107.2 ng/g DM	Anticancer Antioxidant	[21]
				Tetrahydroxy-bufadienolide-dHex isomer 1	Identified		
				Tetrahydroxy-oxo-bufadienolide-acetate isomer 1	186.6 ng/g DM		
				Tetrahydroxy-bufadienolide-dHex isomer 2	Identified		
				Bersaldegenin-acetate/bryophyllin-C isomer 1	35.6 ng/g DM		
				Bryophyllin-B/bryotoxin-B isomer 1	113.4 ng/g DM		
				daigremontianin isomer 1	56.2 ng/g DM		
				Bryophyllin-A/bryotoxin-C isomer 1	573.5 ng/g DM		
				Bryophyllin-B/bryotoxin-B isomer 2	Identified		
				Daigremontianin isomer 2	81.4 ng/g DM		
				Bryophyllin-A/bryotoxin-C isomer 2	Identified		

Table 1. *Cont.*

Plant Part	Extraction Method	Solvent	Detection/Quantification Method	Reported Compound	Identified/Content	Biological Activity Reported	Ref.
Leaves	Maceration	Water	UHPLC-DAD-ESI-MS	Tetrahydroxy-oxo-bufadienolide-acetate isomer 2	Identified	Anticancer Antioxidant	[21]
				Daigremontianin isomer 3	Identified		
				Bryophyllin-A/bryotoxin-C isomer 2	Identified		
				Bersaldegenin-acetate/bryophyllin-C isomer 2	19.2 ng/g DM		
				Daigredorigenin-acetate	2.0 ng/g DM		
				Daigremontianin	399.4 ng/g DM		
				Methyl-daigremonate isomer 1	Identified		
				Methyl-daigremonate isomer 2	Identified		
				Bersaldegenin-1,3,5-orthoacetate	757.4 ng/g DM		
Leaves	Fresh juice after crushing leaves	Not used	UHPLC QTOF-MS	3β-(O-α-L-rhamnopyranosyl)-5β,11α,14 β,19-tetrahydroxybufa-20,22-diene	Identified	Antioxidant	[17]
				Bryophyllin B	Identified		
				Etrahydroxy-bufadiene-O-dHex	Identified		
				Bersaldegenin-acetate isomer 1	Identified		
				Bryotoxin-B	Identified		
				Bryophyllin A/bryotoxin C	5.9 mg/g DM		
				Bersaldegenin-acetate isomer 2	Identified		
				Bryophyllin A/bryotoxin C isomer 2	Identified		
				Diagremontianin isomer	1.9 mg/g DM		

Table 1. *Cont.*

Plant Part	Extraction Method	Solvent	Detection/Quantification Method	Reported Compound	Identified/Content	Biological Activity Reported	Ref.
Leaves	Fresh juice after crushing leaves	Not used	UHPLC QTOF-MS	Bryophyllin –C	3.0 mg/g DM	Antioxidant	[17]
				Diagremontianin	4.6 mg/g DM		
				1,3,5-bersaldegenin-orthoacetate	80.4 mg/g DM		
Leaves	Turbo extraction	Water	UPLC-MS/MS HPTLC	Sagittatin A 4″-Acetylsagittatin A 4″-Acetylsagittatin A Kaempferol 3-(2″-rhamnosyl-6″-acetylgalactoside) 7 rhamnoside 4″-Acetylsagittatin A Highly glycosylated flavonoids	Identified	Not reported	[36]
Leaves	Maceration	Water/ethanol	HPLC-DAD	Cathechin	Identified	Antioxidant	[37]
				Syringic acid	3.44/8.09 µg/g DM		
				Vanillin	3.63/7.99 µg/g DM		
				p-Coumaric acid	3.19/7.90 µg/g DM		
				Sinapic acid	3.85/8.81 µg/g DM		
				Rutin	3.82/8.39 µg/g DM		
				Ellagic acid	Identified		
				Quercetin	7.37/16.51 µg/g DM		
				Chrysine	36.53/79.91 µg/g DM		

Table 1. *Cont.*

Plant Part	Extraction Method	Solvent	Detection/Quantification Method	Reported Compound	Identified/Content	Biological Activity Reported	Ref.
Leaves	Cold pressure of fresh leaves	Not used	SPME/GC/MS	Furan, 2-ethyl Hexanal 2-Hexenal Heptanal 2,4-Hexadienal (E, E) 2 (5 H)—Furanone,5-ethyl Oxalic acid 1-Octen-3-ol Furan, 2-pentyl 1,4-Hexadiene,3-ethyl 1-Hexanol, 2-ethyl Nonanal 2-Nonenal (E) Cyclohexanol,5-methyl-2-(1-methylethyl) Decanal 1-Cyclohexene-1-carboxaldehyde,2,6,6-trimethyl Tetradecane Hexadecane	Identified	Not reported	[12]

Table 1. *Cont.*

Plant Part	Extraction Method	Solvent	Detection/Quantification Method	Reported Compound	Identified/Content	Biological Activity Reported	Ref.
Leaves	Maceration with Ethanol-water (95:5 *v*/*v*)	Bufadienolide- and flavonoid-rich fractions	HPLC-DAD-ESI-MS	Bryophyllin A Bryophyllin C Bersaldegenin-3-orthoacetate Daigremontianin Methyl daigremonate Bersaldegenin-1,3,5-orthoacetate Quercetin O-triglycoside Kaempferol 3-O-xylosyl rhamnoside-7-O-glucoside Myricetin O-diglycoside Myricetin O-hexoside Unknown isoflavone Myricetin O-rhamnoside Unknown flavonoid Isorhamnetin O-diglycoside Quercetin 3-O-glucoside Patuletin O-pentoside Unknown isoflavone Kaempferitrin Isorhamnetin O-hexoside Quercetin 3-O-xylosyl-rhamnoside Kaempferol O-acetyl-rhamnoside Kaempferol 3-O-arabinosyl-rhamnoside isorhamnetin O-diglycoside Kaempferol 3-O-xylosyl-rhamnoside Kaempferol O-diglycoside	Identified	Cytotoxic	[13]

Table 1. *Cont.*

Plant Part	Extraction Method	Solvent	Detection/Quantification Method	Reported Compound	Identified/Content	Biological Activity Reported	Ref.
Leaves	Maceration	Methanol	NMR spectroscopy	Bryophyllin A Bryophyllin C Bersaldegenin-3-acetate Bersaldegenin-1,3,5-orthoacetate Daigremontianin Bersaldegenin-1-acetate Methyl daigremonate	Identified	Insecticidal	[38]
Leaves	Blending extraction	Water	UPLC-MS/MS	Phenolic compounds	50.15 mg/g DM	Antioxidant	[23]
				Flavonoid glycosides	Identified		
Leaves	Maceration with hexane	Tocopherol-rich fraction	HPLC-MS	α–Tocopherol	16.9–24.9 µg/g FW	Not reported	[29]
				γ-Tocopherol	7.9–37.3 µg/g FW		
				δ-Tocopherol	1.1–5.4 µg/g FW		
				γ + ß-Tocomonoenol	1.7–3.1 µg/g FW		
				δ-Tocomonoenol	0.33–0.65 µg/g FW		
Leaves	Maceration with chloroform	Wax fraction	TOF-SIMS	Glutinol	8–12%	Not reported	[39]
				Friedelin	5–9%		
				Triacontanol	<2%		
				n-tritriacontane	<2%		
				Octacosanoic acid	<2%		
Roots	Maceration with water	Bufadienolide-rich fraction	HPLC-MS	1ß,3ß,5ß,14ß,19-pentahydroxybufa-20,22-dienolide	1.07 mg/g DM	Thrombin inhibitory	[40]
				19-(acetyloxy)-1ß,3ß,5ß,14ß-tetrahydroxybufa-20,22-dienolide	13.23 mg/g DM		

Table 1. *Cont.*

Plant Part	Extraction Method	Solvent	Detection/Quantification Method	Reported Compound	Identified/Content	Biological Activity Reported	Ref.
Roots	Maceration with water	Bufadienolide-rich fraction	HPLC-MS	3ß-(O-α-l-rhamnopyranosyl)-5ß,11α,14ß,19-tetrahydroxybufa-20,22-dienolide	9.42 mg/g DM	Thrombin inhibitory	[40]
				19-(acetyloxy)-3ß,5ß,11α,14ß-tetrahydroxybufa-20,22-dienolide	14.13 mg/g DM		
				3ß,5ß,11α,14ß,19-pentahydroxy-12-oxo-bufa-20,22-dienolide	3.78 mg/g DM		
				19-(acetyloxy)-3ß,5ß,11α,14ß-tetrahydroxy-12-oxobufa-20,22-dienolide	8.64 mg/g DM		
				19-(acetyloxy)-1ß,3ß,5ß,11α,14ß-pentahydroxy-12-oxobufa-20,22-dienolide	14.13 mg/g DM		
				1ß-(acetyloxy)-3ß,5ß,11α,14ß,19-pentahydroxy-12-oxobufa-20,22-dienolide	Identified		
				11α,19-dihydroxytelocinobufagin (3ß,5ß,11α,14,19-pentahydroxybufa-20,22-dienolide)	7.23 mg/g DM		
				Bersaldegenin 1-acetate	1.59 mg/g DM		
				Daigredorigenin 3-acetate	4.13 mg/g DM		
				Bersaldegenin 1,3,5-orthoacetate	29 mg/g DM		
				Bryotoxin B	10.64 mg/g DM		
				Bryophyllin B	1.47 mg/g DM		

Table 1. *Cont.*

Plant Part	Extraction Method	Solvent	Detection/Quantification Method	Reported Compound	Identified/Content	Biological Activity Reported	Ref.
Roots	Maceration with water	Bufadienolide-rich fraction	HPLC-MS	Bersaldegenin	1.75 mg/g DM	Thrombin inhibitory	[40]
				Hellebrigenin 3-acetate	1.37 mg/g DM		
				Hovetrichoside C	28.17 mg/g DM		
				Schisandriside	14.13 mg/g DM		
				(7S-8R)-dihydrodehydrodiconiferyl-alcohol-3-O-glucoside	2.67 mg/g DM		
				(7R-8S)-dihydrodehydrodiconiferyl-alcohol-3-O-glucoside	2.67 mg/g DM		
Roots	Maceration	Bufadienol-rich fraction	UPLC-MS	11α,19-dihydroxytelocinobufagin bersaldegenin-1-acetate	0.06 mg/g DM	Antioxidant Cytotoxic	[27]
				Bersaldegenin-1	0.051 mg/g DM		
				3,5-orthoacetate	0.064 mg/g DM		
				19-acetyloxy-11α-hydroxy-12-oxo-telocinobufagin	0.068 mg/g DM		
				19-acetyloxy-1b-hydroxytelocinobufagin	0.068 mg/g DM		
Roots	Ultrasonic waves	Water	HPLC-ESI-MS NMR spectroscopy	1β,3β,5β,14β,19-pentahydroxybufa-20,22-dienolide	5.3 µg/g DM	Not reported	[10]
				19-(acetyloxy)-1β,3β,5β,14β -tetrahydroxybufa-20,22-dienolide	11.2 µg/g DM		
				3β-O-α-L-rhamno-pyranosyl-5β,11α,14β,19-tetrahydroxybufa-20,22-dienolide	11 µg/g DM		

Table 1. *Cont.*

Plant Part	Extraction Method	Solvent	Detection/Quantification Method	Reported Compound	Identified/Content	Biological Activity Reported	Ref.
Roots	Ultrasonic waves	Water	HPLC-ESI-MS NMR spectroscopy	19-(acetyloxy)-3β,5β,11α,14β -tetrahydroxybufa-20,22-dienolide	6.1 µg/g DM	Not reported	[10]
				3β,5β,11α,14β,19-pentahydroxy-12-oxo-bufa-20,22-dienolide	15.4 µg/g DM		
				19-(acetyloxy)-3β,5β,11α,14_-tetrahydroxy-12-oxo-bufa-20,22-dienolide	25 µg/g DM		
				19-(acetyloxy)-1β,3β,5β,11α,14β-pentahydroxy-12-oxo-bufa-20,22-dienolide	6 µg/g DM		
				1β-(acetyloxy)-3β,5β,11α,14β,19-pentahydroxy-12-oxo-bufa-20,22-dienolide	14.7 µg/g DM		
				11α,19-dihydroxytelocinobufagin	4.8 µg/g DM		
				Bersaldegenin-1-acetate	4.6 µg/g DM		
				Daigredorigenin-3-acetate	9.5 µg/g DM		
				Bersaldegenin-1,3,5-orthoacetate	25.8 µg/g DM		
				Bryotoxin B	6.4 µg/g DM		
				Bryophyllin B	8.5 µg/g DM		
				Bersaldegenin	6.2 µg/g DM		

Table 1. *Cont.*

Plant Part	Extraction Method	Solvent	Detection/Quantification Method	Reported Compound	Identified/Content	Biological Activity Reported	Ref.
Flowers	Maceration	Acidified methanol	TOF-MS	Delphinidin 3-O-glucoside Pelargonidin-3-glucoside Cyanidin-3-glucoside	Identified	Antioxidant	[34]
No information	Extraction of wax	Lipidic fraction	TLC/Gravimetric method	Fatty acids	45.4 mg/100 g FW	Antihemolytic Antimicrobial	[30]
				β-carotene	2.6 mg/100 g FW		
				Chlorophylls	60.6 mg/100 g FW		
				Carotenoids	19.6 mg/100 g FW		
				Sterols	16.4 mg/100 g FW		
				Sterol ethers	9.8 mg/100 g FW		
				Fatty acid ethers	21 mg/100 g FW		
				Triacylglicerols	38 mg/100 g FW		
				Monogalactosyl diglyceride	9 mg/100 g FW		
				Sulfochinovosyl diglycerine	9.8 mg/100 g FW		
				Phospholipids	13.4 mg/100 g FW		

DM: Dry Matter; FW: Fresh Weight; HPLC: High-Performance Liquid Chromatography; HPLC-PDA: High-Performance Liquid Chromatography with Photo Diode Array Detection; NMR: Nuclear Magnetic Resonance; TLC: Thin Layer Chromatography; HPLC-DAD: High-Performance Liquid Chromatography with Diode Array Detection; LC–ESI-MS/MS: Liquid Chromatography–Electrospray Ionization–Tandem Mass Spectrometry; TOF-MS: Time-of-Flight Mass Spectrometry; NMR: Nuclear Magnetic Resonance; UHPLC-DAD-MS: Ultra-High Performance Liquid Chromatography—Diode Array Detector—Mass Spectrometry; UHPLC-DAD-ESI-MS: Ultra-high-performance liquid chromatography diode array detector electrospray ionization tandem mass spectrometry; UHPLC: Ultra-High-Performance Liquid Chromatography; QTOF-MS: Quadrupole Time-of-Flight Mass Spectrometry; SPME/GC/MS: Solid-Phase Microextraction/Gas Chromatography/Mass Spectrometry; UPLC-MS/MS: Ultra-Performance Liquid Chromatography-Tandem Mass Spectrometry; TOF-SIMS: Time-of-Flight Secondary Ion Mass Spectrometry.

Polyphenolic compounds are metabolites derived from secondary plant pathways, playing essential roles in plant growth, development, and defense mechanisms. These compounds are characterized by an aromatic benzene ring and at least one hydroxyl group in their structure [41]. These compounds are classified as phenolic acids, flavonoids, tannins, stilbenes, and lignans based on their chemical structure [42]. Notably, *K. daigremontiana* leaves contain significant amounts of phenols, ranging from 0.1482 to 50.15 mg/g, while flavonoid levels have been reported at 7.35 and 17.35 mg/g [19,23,31]. Furthermore, the phenolic acids and flavonoids identified in *K. daigremontiana* leaves include gallic, chlorogenic, γ-resorcylic, p-coumaric, ferulic, caffeic, syringic, protocatechuic, sinapic, and ellagic acids, as well as kaempferol, catechin, rutin, quercetin, myricetin, delphinidin 3-O-glucoside, pelargonidin-3-glucoside, cyanidin-3-glucoside, and chrysene [11,20,34,37]. These compounds are highlighted by their antioxidant, anti-inflammatory, and antimicrobial properties [19,23,31].

Bufadienolides are the most extensively studied phytochemicals in *Kalanchoe* species, particularly in the leaves and roots of *K. daigremontiana* [10,13,21,27,35,38,43–45]. These compounds are characterized by a steroid nucleus (cyclopentanoperhydrophenanthrene) linked to a six-membered lactone ring (α-pyron) at the C-17β position [25,46]. Over 40 bufadienolide compounds have been identified in the leaves and roots of *K. daigremontiana* [17,47]. According to the literature, these compounds have been identified in aqueous, ethanolic, methanolic, and dichloromethane extracts or fractions [5,21,24,27,38,46,48]. Among these, 19-(acetyloxy)-1ß,3ß,5ß,11α,14ß-pentahydroxy-12-oxobufa-20,22-dienolide, 19-(acetyloxy)-3ß,5ß,11α,14ß-tetrahydroxybufa-20,22-dienolide, and 19-(acetyloxy)-1ß,3ß,5ß,14ß -tetrahydroxybufa-20,22-dienolide showed the highest reported concentration [40]. Various studies have reported that these compounds exhibited cytotoxic, antitumor, cardiotonic, and analgesic properties [49,50].

Given the widespread use of *K. daigremontiana* in both traditional medicine and scientific research, a comprehensive phytochemical analysis is warranted to elucidate its potential applications.

4. Biological Activities of Extracts from *Kalanchoe daigremontiana*

Kalanchoe daigremontiana has been used as a medicinal plant to treat various health conditions [3]. Given its widespread and popular use, scientific research has been conducted to corroborate its pharmaceutical potential. Studies report that its leaf and root extracts possess antioxidant, antimicrobial, anti-inflammatory, thrombin-inhibitory, hepatoprotective, anti-aging and skincare, cardiac glycoside-like, and anticancer properties, as discussed below.

Among the 44 reports that evaluated the biological activities of *K. daigremontiana* reviewed for this manuscript, approximately 80% corresponded to in vitro studies and 20% to in vivo studies, including murine, poultry, goat, and *Artemia salina*. Regarding the plant part used, 92.5% corresponded to leaves, and the remaining to roots. Regarding the extraction methods, 47.72% involved maceration in organic solvents, and the remaining methods were magnetic stirring, the Soxhlet method, ultrasonic waves, cold pressure, percolation, lixiviation, leaching, and homogenization. The most common solvents were water (29.54%), ethanol (29.54%), and methanol (25%); the remaining fractions comprised dichloromethane, carbon tetrachloride, and bufadienolide-rich fractions. Additionally, most in vitro studies are antioxidant evaluations (31.37%), cytotoxicity studies (27.49%), and antimicrobial studies (19.6%). The remaining 23.54% were evaluated for anti-inflammatory, anticoagulant, anti-aging, hepatoprotective, and skin-care properties, among others. The research groups that have studies *K. daigremontiana* are predominantly from Poland [5,27,35], Mexico [6,8,16], Russia [30], Brazil [32], and Indonesia [38], among others.

4.1. Antioxidant

Kalanchoe daigremontiana is recognized as a significant source of antioxidant compounds [11]. The pharmacological significance of these compounds is attributed to their capacity to neutralize reactive species, thereby mitigating oxidative-induced cellular damage associated with the pathogenesis of non-communicable diseases, such as diabetes, cardiovascular conditions, neurological disorders, and cancer [21]. As summarized in Table 2, leaves are the primary site for extracting antioxidant compounds, typically via maceration. Nonetheless, other methods, such as high-speed blending, percolation, and magnetic stirring, have been used for extraction. While polar solvents such as ethanol, methanol, and aqueous systems are commonly used, some studies have investigated the use of isopropanol and solvent partitioning to isolate high-purity fractions. Typically, the extracts are concentrated through rotary evaporation and subsequently resuspended in water prior to analysis. Methodologically, antioxidant quantification has been documented across a broad concentration range from 1 μg/mL to 450 mg/mL, utilizing a comprehensive array of in vitro assays, including DPPH (2,2-diphenyl-1-picrylhydrazyl), ABTS (2,2′-Azinobis(3-ethylbenzothiazoline-6-sulfonic acid), and superoxide and nitric oxide radicals, FRAP (ferric reducing assay power), and ORAC (oxygen radical absorbance capacity).

Maltok et al. [51] reported that the *K. daigremonitiana* plant is a good source of antioxidant compounds. The filtered juice obtained after crushing the leaves of *K. daigremontiana* demonstrated moderate antiradical activity against DPPH and ABTS radicals, as well as low ferric and molybdenum reducing capabilities [17]. Notably, the macerated extract showed higher antioxidant activity in the ABTS assay than in the DPPH assay [19]. Ethanolic extracts obtained through maceration of *K. daigremontiana* leaves showed DDPH radical scavenging activity up to 66.89% in a concentration-dependent manner (25–200 μg/mL), with an EC_{50} value of 145 μg/mL [52].

Bogucka-Kocka et al. [11] observed similar trends, reporting up to 80% inhibition of DPPH radical, with an EC_{50} value of 180 μg/mL. Additionally, this extract demonstrated antioxidant activity against superoxide radicals (50% of inhibition; EC_{50} of 56.2 μg/mL) and nitric oxide radicals (100% of inhibition; EC_{50} of 270 μg/mL). The authors agree that these antioxidant effects are attributed to the concentration and type of bioactive compounds present in the extracts, noting the presence of benzoic and caffeic acid derivatives [11]. Furthermore, it has been documented that macerated aqueous extracts from *K. daigremonitiana* leaves exhibited higher antioxidant activity in the FRAP assay (IC_{50}: 1271 μg/mL) than in the DPPH assay (IC_{50}: 1750 μg/mL), highlighting the influence of phytochemical composition and concentration on antioxidant activity [21]. Furthermore, ethanol, hexane, dichloromethane, butanol, and water fractions obtained from *K. daigremontiana* leaves exhibited antioxidant properties against DPPH and ABTS radicals and anti-lipid peroxidation activity [53].

Additionally, Elizondo-Lluevano et al. [54] reported that the macerated methanolic extract exhibited strong inhibitory activity against the DPPH radical (IC_{50}: 19.2 μg/mL), attributed to its flavonoid content, which was comparable to that of Vitamin E (IC_{50}: 16.9 μg/mL).

Table 2. Antioxidant activity reported in *Kalanchoe daigremontiana*.

Plant Part	Extraction/Extract Conditioning	Solvent Extraction	Resuspension/ Fractionation	Concentration	Model Assay	Relevant Results	Ref.
Leaves	NI	NI		Direct quantification	DPPH ABTS	Plants are a source of antioxidant compounds	[51]
Leaves	Fresh juice after crushing leaves (After extraction and evaporation at 40 °C, lyophilized)	Not used	No information	0.6–450 mg/mL	DPPH ABTS FRAP Molybdenum reducing power	The juice exhibited moderate dose-dependent antioxidant capacity	[17]
Leaves	Maceration in a juice extractor	Not used	Not used	Direct quantification	DPPH ABTS	The antioxidant activity was higher for ABTS than for DPPH	[19]
Leaves	Maceration	Ethanol 70%	No information	25–200 µg/mL	DPPH	The inhibition (10.81 to 66.89%) of DPPH radical was concentration dependent, with an EC_{50} value of 145 µg/mL	[52]
Leaves	Maceration (Collected extracts were vacuum concentrated to dryness)	96% ethanol	The residues were dissolved in HPLC-grade water prior to analysis	1–1000 µg/mL	DPPH Superoxide radical Nitric oxide radical	The antioxidant capacity was dependent on the concentration and the antiradical method	[11]
Leaves	Maceration (Extract was filtered, concentrated by rotary evaporation at 40 °C, and lyophilized.)	Water	The dried extract was dissolved in distilled water prior to analysis	0.04–2.5 mg/mL	DPPH FRAP	The antioxidant activity was higher for FRAP than for DPPH	[21]
Leaves	Maceration (Extract was concentrated by rotary evaporation at 60 °C up to dryness)	Water Ethanol 70%	No information	31.5 mg/mL 70 mg/mL	NI	The extracts improve the stability of vegetable oil during storage	[37]

Table 2. *Cont.*

Plant Part	Extraction/Extract Conditioning	Solvent Extraction	Resuspension/ Fractionation	Concentration	Model Assay	Relevant Results	Ref.
Leaves	Maceration (Extracts were dried)	Ethanol	Fractions: Ethanol Hexane Dichloromethane Butanol Water	NI	DPPH ABTS Total antioxidant activity Anti-lipid peroxidation activity	All fractions exhibited antioxidant activity	[53]
Leaves	Maceration (Extract was concentrated using a rotary evaporator)	Methanol	No information	20–2500 µg/mL	DPPH	The extract exhibited good antioxidant properties with IC50 values of 19.2 µg/mL	[54]
Leaves	Grinding in a high-speed blender (Extract was filtered and freeze-dried)	Water	No information	40–400 µg/mL	DPPH ABTS	The aqueous extract exhibited antioxidant capacity	[23]
Leaves	Grinding in a high-speed blender (Aqueous extract was freeze-dried, ethanolic and isopropanolic extracts were concentrated by rotatory evaporator up to dryness)	Water Ethanol Isopropanol	No information	Direct quantification	ORAC ABTS	The antioxidant activity was dependent on the solvent used; isopropanol > ethanol > water	[55]
Leaves	Magnetic stirring (Extracts were concentrated by rotary evaporation)	Ethanol 50% Ethanol 70% Ethanol 80% Methanol 80%	No information	5 mg/mL	DPPH	The extract exhibited antioxidant properties	[56]

Table 2. *Cont.*

Plant Part	Extraction/Extract Conditioning	Solvent Extraction	Resuspension/ Fractionation	Concentration	Model Assay	Relevant Results	Ref.
Leaves	Maceration (Extracts were concentrated by rotary evaporation)	Water Ethanol Petrol ether	All extracts were dissolved in DMSO at different concentrations	1000 µg/mL	DPPH Superoxide radical Nitric oxide radical	The extract exhibited antioxidant activity in the DPPH test, but not for superoxide and nitric oxide radicals	[14]
Leaves	Percolation (Extract was concentrated)	Methanol	Redissolved in ethanol and stored at 4 °C	Direct quantification	DPPH ABTS	The antioxidant activity was higher for DPPH than ABTS	[34]
Leaves	Lixiviation (Filtered and concentrated using rotary vapor up to dryness)	Ethanol 78%	No information	Direct quantification	ABTS	The extract exhibited antioxidant properties	[57]
Roots	Maceration (Extract was concentrated and lyophilized)	Water	Bufadienolide-rich fraction	1–100 µg/mL	DPPH FRAP	The fraction exhibited antioxidant properties in the used assay models	[27]

DPPH: 2,2-diphenyl-1-picrylhydrazyl radical; ABTS: 2,2′-Azino-bis(3-ethylbenzothiazoline-6-sulfonic acid) radical cation; FRAP: Ferric reducing assay power; ORAC: Oxygen radical absorbance capacity.

de Andrade et al. [23] demonstrated that the *K. daigremontiana* leaf aqueous extract obtained through a high-speed blender exhibited superior antioxidant activity in the ABTS assay (193.61 μg/mL) compared to the DPPH assay (>1000 μg/mL). Furthermore, employing the same extraction technique, it has been documented that isopropanol extracts from *K. daigremontiana* leaves showed enhanced antioxidant activity in both DPPH and ORAC assays (3000 and 900 μmol Trolox equivalent/μg extract, respectively) compared to ethanolic (1200 and 700 μmol Trolox equivalent/μg extract) and aqueous (300 μmol Trolox equivalent/μg extract) extracts [55]. These results were attributed to the expected amount and type of bioactive compounds extracted by each solvent [23,55].

Baéz et al. [56] demonstrated that the 70% ethanolic extract (IC_{50}: 3.01 μg/mL) derived from *K. daigremontiana* leaves through magnetic stirring exhibited superior DPPH radical inhibition compared to the 50% ethanol (IC_{50}: 4.41 μg/mL), 80% ethanol (IC_{50}: 3.80 μg/mL), and 80% methanol (IC_{50}: 3.51 μg/mL) extracts. Similarly, Quintero et al. [14] observed that the aqueous extract obtained via magnetic stirring from *K. daigremontiana* leaves at a concentration of 1000 μg/mL showed low to moderate inhibitory effects against the DPPH radical (34.7%), with no inhibition detected for superoxide and nitric oxide radicals. Additionally, the methanolic extract obtained by percolation from *K. daigremontiana* leaves demonstrated inhibitory activity against both DPPH and ABTS radicals [34]. Paitan et al. [57] reported that extracts from *K. daigremontiana* leaves obtained through lixiviation exhibited inhibitory activity against ABTS radical cation. Additionally, Kolodziejczyk-Czepas et al. [27] evaluated the antioxidant activity of a bufadienolide-rich fraction isolated from *K. daigremontiana* roots in DPPH radical and blood plasma in vitro. In the DPPH assay, the fraction exhibited an EC_{50} of 21.8 μg/mL. In the blood plasma model under peroxynitrite-induced oxidative stress, the extract exhibited moderate antioxidant activity and no cytotoxic effects at concentrations ranging from 1 to 50 μg/mL.

K. daigremontiana leaves and roots are a source of antioxidant compounds because they can inhibit the formation of free radicals harmful to human cells and have a key role in protecting against diverse chronic non-communicable diseases, such as diabetes, cardiovascular conditions, and cancer. This evidence could support the use of *K. daigremontiana* as a medicinal plant for treating oxidative stress-related diseases.

4.2. Antimicrobial

In traditional medicine, *K. daigremontiana* is extensively used to treat infectious diseases, including parasitic, viral, and bacterial infections [4]. In research studies, the leaves of *K. daigremontiana* are primarily used for antimicrobial purposes, including antibacterial, antifungal, antiviral, antiparasitic, and anthelmintic, as shown in Table 3. For antimicrobial purposes, ethanol, methanol, and aqueous extracts are commonly utilized; these extracts are typically concentrated through rotary evaporation up to dryness and subsequently resuspended in water, dimethyl sulfoxide (DMSO), and methanol, as well as fractionated with *n*-hexane, carbon tetrachloride, and chloroform, which are dried and resuspended prior to analysis. For the antibacterial activity of *K. daigremontiana* leaf extracts, disk diffusion and microdilution are the most used analytical methods. Using the disk diffusion method, Anisimov et al. [30] reported that the ethanolic extract of *K. daigremontiana* leaves (5 mg/mL) obtained by homogenization exhibited antibacterial activity against *Escherichia coli* (4 mm of inhibition) and *Staphylococcus aureus* (6 mm of inhibition).

Table 3. Antimicrobial activity of *Kalanchoe daigremontiana* extracts.

Activity	Plant Part	Extraction/Extract Conditioning	Solvent	Resuspension/ Fractionation	Concentration	Microorganisms	Model Assay	Relevant Results	Ref.
Antibacterial	Leaves	Maceration (Extract was concentrated by rotary evaporator at 40 °C, followed by fractionation)	Ethanol 95%	Aqueous and dichloromethane fractions were filtered, concentrated up to dryness, and lyophilized prior to use	9 to 0.0035 mg/mL	*Streptococcus* β-hemolyzing group A *Streptococcus* β-hemolyzing group G *Corynebacterium diphtheriae* *Staphylococcus aureus* *Staphylococcus epidermidis* *Clostridium sporogenes* *Clostridium bifermentans* *Cutibacterium acnes* *Streptococcus equinus* *Helicobacter pylori*	Broth microdilution	The extract exhibited antibacterial activity against all evaluated microorganisms, but effectiveness was dependent on the strain, extract concentration, and type of fraction	[5]
Antibacterial	Leaves	Maceration (Extract was concentrated by rotary evaporator, followed by fractionation)	Methanol	*n*-hexane, carbon tetrachloride, chloroform, and aqueous fractions were dried and resuspended	300 µg/disk	*Bacillus cereus* *Bacillus megaterium* *Bacillus subtilis* *Staphylococcus aureus* *Sarcina lutea* *Escherichia coli* *Pseudomonas aeruginosa* *Salmonella* Paratyphi *Salmonella* Typhi *Shigella boydii* *Shigella dysenteriae* *Vibrio mimicus* *Vibrio parahemolyticus*	Disk diffusion	The extract exhibited antibacterial activity against all evaluated microorganisms, but effectiveness was dependent on the strain	[58]
Antibacterial	Leaves	Leaching (Extract was filtered and concentrated by rotary evaporator)	Ethanol 78%	No information	NI	*Escherichia coli* *Staphylococcus aureus* *Pseudomonas aeruinosa* *Salmonella* Enteritidis	Disk diffusion	The extract exhibited antibacterial activity against all evaluated microorganisms, but effectiveness was dependent on the strain	[57]
Antibacterial	Leaves	Maceration (Extract was concentrated by rotatory evaporator)	Methanol	Resuspended in methanol	1.5 mg/mL	*Salmonella* Typhi	Disk diffusion	The extract showed an inhibition of 41.7%	[8]

Table 3. *Cont.*

Activity	Plant Part	Extraction/Extract Conditioning	Solvent	Resuspension/ Fractionation	Concentration	Microorganisms	Model Assay	Relevant Results	Ref.
Antibacterial	Leaves	Maceration (Extract was concentrated in a rotary evaporator up to dryness)	Methanol-water 30–70%	No information	100 mg/mL	*Listeria monocytogenes* *Salmonella* Typhimurium *Pseudomonas aeruinosa* *Salmonella* Choleraesuis *Bacillus subtilis* *Escherichia coli* *Staphylococcus aureus*	Broth microdilution	The antibacterial effects were dependent on the bacterial species and the concentration of the extract	[6]
Antibacterial	NI	Homogenization (Extract was filtered and concentrated in a rotary evaporator)	Ethanol 96%	No information	5 mg/mL	*Escherichia coli* *Staphylococcus aureus*	Disk diffusion	The extract showed antibacterial properties against *E. coli* and *S. aureus*	[30]
Antifungal	Leaves	Maceration (Extract was concentrated in a rotary evaporator, following fractionation)	Methanol	*n*-hexane, carbon tetrachloride, chloroform, and aqueous fractions were dried and resuspended	300 µg/disk	*Candida albicans* *Aspergillus niger* *Saccharomyces cerevisiae*	Disk diffusion	The extracts showed antifungal activity, but effectiveness varied by strain. No effects were detected in *S. cerevisiae*	[58]
Antifungal	NI	Homogenization (Extract was filtered and concentrated in a rotary evaporator)	Ethanol 96%	No information	5 mg/mL	*Safale S-04* *Candida albicans* *Aspergillus niger*	Well diffusion	The extracts showed antifungal activity, but effectiveness varied by strain. No effects were detected in *A. niger*	[30]
Antifungal	Leaves	Maceration (Extract was concentrated by rotary evaporator at 40 °C, followed by fractionation)	Ethanol 95%	Aqueous and dichloromethane fractions were filtered, concentrated up to dryness, and lyophilized prior to use	9 to 0.0035 mg/mL	*Candida albicans*	Broth microdilution	No significant effects were observed on *C. albicans* inhibition	[5]
Antiviral	Leaves	Maceration	Water	No information	1–160 mg/mL	Human herpesvirus type 1 (HHV-1)	qPCR	The extract reduces viral infection in a concentration-dependent manner	[35]

Table 3. *Cont.*

Activity	Plant Part	Extraction/Extract Conditioning	Solvent	Resuspension/ Fractionation	Concentration	Microorganisms	Model Assay	Relevant Results	Ref.
Antiviral	Leaves	Grinding in a high-speed blender (Extract was concentrated by evaporation)	Water	No information	HSV-1: EC_{50}: 0.97 µg/mL HSV-2 EC_{50}: 0.72 µg/mL	Human herpesvirus type 1 (HHV-1) Human herpesvirus type 2 (HHV-2)	PCR	The extract exhibited antiviral properties against HHV-1 and HHV-2	[32]
Antiparasitic	Leaves	Maceration (Concentrated using a rotary evaporator)	Methanol	Extract resuspended at 1 mg/mL in 0.5% (*w*/*v*) DMSO	LC_{50}: 70.71 µg/mL LC_{50}: 105.27 µg/mL	*Entamoeba histolytica Trichomonas vaginalis* (trophozoites form)	Microassay technique	The extract showed antiparasitic activity against trophozoites of *E. istolytica* and *T. vaginalis* in their trophozoite phases	[54]
Antiparasitic	Leaves	Maceration (Extract was filtered and concentrated using a rotary evaporator)	Methanol	Extract was resuspended in DMSO (≤5%)	LC_{50}: 70.71 µg/mL LC_{50}: 105.27 µg/mL	*Entamoeba histolytica Trichomonas vaginalis* (logarithmic phase)	Microassay technique	The extract showed antiparasitic activity against trophozoites of *E. istolytica* and *T. vaginalis* in their logarithmic phases	[16]
Anthelmintic	Leaves	Maceration (Extract was concentrated in a rotary evaporator)	Methanol-water 30–70%	No information	Egg hatching LC_{50}: 66.5 mg/mL LC_{90}: 87.3 mg/mL	*Haemonchus contortus* eggs collected from the feces of infected lambs	ELISA	The extract inhibits the egg hatching (99.5%) and reduces the motility of larvae (85% at 400 mg/mL	[6]

DMSO: dimethyl sulfoxide; EC_{50}: half maximal effective concentration; LC_{50}: mean lethal concentration.

Additionally, it has been reported that ethanolic extract obtained by leaching showed antibacterial properties in a strain-dependent manner, where *Pseudomonas aeruginosa* (18.6 mm of inhibition) was more sensitive to the extract, followed by *S. aureus* (13 mm of inhibition), *Salmonella* Enteriditis (11.7 mm of inhibition), and *Escherichia coli* (11.7 mm of inhibition) [57]. Nahar et al. [58] evaluated the effectiveness of different partitioned extracts (n-hexane, chloroform, methanol, and carbon tetrachloride) from *K. daigremontiana* leaves against a variety of Gram-positive (*Bacillus cereus*, *Bacillus megaterium*, *Bacillus subtilis*, *Staphylococcus aureus*, and *Sarcina lutea*) and Gram-negative (*E. coli*, *P. aeruginosa*, *S.* Paratyphi, *S.* Typhi, *Shigella boydii*, *S. dysenteriae*, *Vibrio mimicus*, and *V. parahemolyticus*) bacteria. They reported that the antibacterial effects of partitioned extractives from n-hexane, chloroform, and methanol were dependent on the bacterial strain. In contrast, the carbon tetrachloride partitioned extract exhibited strong antibacterial activity against all evaluated strains (9 to 14 mm of inhibition); these results were compared with standard kanamycin, which showed inhibition zones from 10 to 18 mm depending on the evaluated strain. Furthermore, it has been reported that the methanolic extract from *K. daigremontiana* leaves (evaporated to dryness and resuspended in methanol) can inhibit the growth of *S.* Typhi up to 41.7%, compared with chloramphenicol control [8].

Rivero-Pérez et al. [6] evaluated the antibacterial effect of methanol-water extract from K. daigremontiana leaves against *E. coli*, *Salmonella* Typhimurium, *Salmonella* Choleraesuis, *Pseudomonas aeruginosa*, *Listeria monocytogenes*, *Bacillus subtilis*, and *Staphylococcus aureus* by microdilution assay, calculating the minimum inhibitory concentration values (MIC) They reported that the extract showed no activity against *E. coli*, *S.* Typhimurium, or *S.* Choleraesuis; low activity against *P. aeruginosa* and *L. monocytogenes* (MIC of 100 mg/mL); and strong activity against *B. subtilis* and *S. aureus* (MIC of 0.781 mg/mL); these results were compared to standard kanamycin, which showed MIC values ranged from 1 to 64 μg/mL in a strain-dependent response. The authors concluded that Gram-positive bacteria are more sensitive to the extract than Gram-negative bacteria, possibly due to differences in cell membranes. For its part, the water and dichloromethane fraction obtained from ethanolic extracts from *K. daigremontiana* exhibited antibacterial activity against a variety of bacterial strains (*Streptococcus* β-hemolyzing group A, *Streptococcus* β-hemolyzing group G, *Corynebacterium diphtheriae*, *S. aureus*, *Staphylococcus epidermidis*, *Clostridium sporogenes*, *Clostridium bifermentans*, *Cutibacterium acnes*, *Streptococcus equinus*, and *Helicobacter pylori*); however, its effects was in bacterial strain-dependent response and solvent fraction, with MIC values of 0.064 to >9.0 mg/mL for water fractions and 0.125 to >2.0 mg/mL for dichloromethane fractions. The most sensitive bacteria were *S. epidermidis* (MIC of 0.064 mg/mL) for the water fraction and *C. sporogenes* (MIC of 0.125 mg/mL) for the dichloromethane fraction; these results were compared to ampicillin, which showed MIC values ranging from 6.3×10^{-5} to 0.016 mg/mL [5]. Conversely, in a previous study, it has been reported that a bufadienolide-rich fraction from water extract (MIC: >50 μg/mL) of *K. daigremontiana* leaves exhibited higher antibacterial activity than derived from ethanol extracts (MIC: 98.4–787 μg/mL) against β-Hemolytic *Streptococcus* group A, β-Hemolytic *Streptococcus* group G, *C. diphtheriae*, *S. aureus*, *S. epidermidis*, *Enterococcus hirae*, and *E. coli*; these results were compared to ampicillin, which showed MIC values ranged from <0.03 to 0.3125 μg/mL [59].

The antifungal activity of *K. daigremontiana* extracts has been evaluated against molds (*Aspergillus niger*) and yeasts (*Candida albicans*, *Saccharomyces cerevisiae*, and *Safale S-04*) in model systems. It has been reported that ethanolic extract (5 mg/mL) from *K. daigremontiana* exhibited antifungal properties against *Safale S-04* and *C. albicans,* but not for *A. niger*; these results were compared to Nitrofungin® [30]. On the other hand, it has been reported that partitioned extractive with carbon tetrachloride from macerated methanolic extract

showed antifungal activity against *C. albicans* and *A. niger,* but not for *S. cerevisiae* [58]. For its part, it has been reported that the dichloromethane fraction obtained from macerated methanolic extracts from *K. daigremontiana* leaves can inhibit the *C. albicans* growth (MIC: 2 mg/mL) [5], whereas the water extract from showed strong inhibitory effects against *C. albicans* (>50 μg/mL); these values were higher than standard amphotericin, which showed MIC values ranged from 0.06 to 0.01 μg/mL [59].

Regarding antiviral properties of *K. daigremontiana* leaves, Gomes-Ürményi et al. [32] reported that the ethyl acetate fraction obtained from macerated methanolic extract exhibited strong inhibitory effects against Human herpesvirus type 1 (HHV-1; EC_{50}: 0.97 μg/mL) and Human herpesvirus type 2 (HHV-2; EC_{50}: 0.72 μg/mL). Furthermore, it has been reported that macerated aqueous extract from *K. daigremontiana* leaves shows an ability to prevent HHV-1 infection by direct inhibition of the virus attachment, penetration, and blocking of infection when used in pretreatment or post-entry treatment; these effects were observed in a concentration-dependent response (1–160 mg/mL) [35]. The antiviral activity was attributed to the phenolic acids and bufadienolides present in the extracts [32].

The antiparasitic and anthelmintic properties of *K. daigremontiana* leaf extracts have also been investigated [6,16,54]. Elizondo-Lluevano et al. [54] evaluated the effect of macerated methanolic extract on trophozoites from *Entamoeba histolytica* and *Trichomonas vaginalis,* important parasites that directly impact public health. They reported that the extract exhibited antiparasitic properties with LC_{50} values of 70.71 and 105.27 μg/mL, respectively; these values were compared to metronidazole, which showed MIC values of 0.17 and 0.09 μg/mL, respectively. Similar trends were observed when evaluating this extract against these parasites in their logarithmic growth phase [16]. Additionally, the macerated methanolic-water extract from *K. daigremontiana* leaves exhibited anthelmintic properties against *Haemonchus contortus* eggs collected from feces from infected lambs. The extract inhibited 99.5% of *H. contortus* eggs from hatching and reduced the motility of 85.2% of L3 larvae (400 mg/mL), with LC_{50} values of 66.5 mg/mL and 1.5 mg/mL for hatching eggs and the inhibition of motility, respectively; these results were compared to Ivermectin 5, which showed 100% of egg hatching inhibition and mortality [6].

According to these data, the extracts from *K. daigremontiana* leaves exhibited antibacterial, antifungal, antiviral, antiparasitic, and anthelmintic properties. Although these effects depended on the type of extract and concentration, as well as microbial strain, results supported the traditional uses of *K. daigremontiana* leaves to treat microbial infections.

4.3. Anti-Inflammatory

Inflammation is the body's primary biological response, serving as a defense mechanism against pathogens, allergens, and injuries that may lead to tissue damage and dysfunction. This process is a critical factor in the pathogenesis of a diverse array of diseases, including bacterial infections, cardiovascular disorders, metabolic syndromes, autoimmune diseases, neurodegenerative disorders, and cancer [60,61]. In this context, it has been reported that extracts from *K. daigremontiana* leaves exhibited in vitro and in vivo anti-inflammatory properties [14,56].

The ethanolic extract from the aerial parts of *K. daigremontiana* has demonstrated the ability to inhibit 50% (IC_{50}) of LOX enzyme activity at a concentration of 21.96 μg/mL [56]. The lipoxygenase (LOX) pathway facilitates the incorporation of molecular oxygen into arachidonic acid, leading to the production of unsaturated hydroperoxides [62]; these compounds act as precursors to potent inflammatory mediators, such as leukotrienes, which play critical roles in promoting chemotaxis and vasodilation, enhancing the inflammatory response by attracting and activating immune cells [62,63]. For its part, Quintero et al. [14] in a carrageenan-induced rat paw edema model reported that both aqueous (0.782 mL,

7 h) and petroleum ether (0.762 mL, 3 h) extracts from *K. daigremontiana* leaves exhibited anti-inflammatory properties, reducing inflammation by 105.69% and 79.95%, respectively, which were comparable to those observed with diclofenac in the positive control group. According to the authors, the anti-inflammatory effects were associated with the presence of steroidal compounds.

4.4. Anticoagulant

The anticoagulant properties of plant-derived compounds have been extensively investigated over recent decades as potential adjuvant or preventive anti-thrombotic therapies. In this regard, Kolodziejczyk-Czepas et al. [40] assessed the in vitro inhibitory effect of a bufadienolide-rich fraction from *K. daigremonitiana* roots (1 to 50 μg/mL) on the enzymatic activity of serine proteinase-thrombin (plasma coagulation factor II). The study reported that the fraction in question reduced the amidolytic (IC_{50} value of 2.79 μg/mL) and proteolytic activity of thrombin (isolated fibrinogen polymerization: IC_{50} of 2.18 μg/mL and fibrinogen polymerization in blood plasma: IC_{50} of 11.32 μg/mL), with results surpassing those of the reference compound argatroban (IC_{50} values: 0.78, 0.003, and 0.029 μg/mL, respectively). The thrombin-inhibitory effect was attributed to the bioactivity of bufadienolide compounds, which act as uncompetitive inhibitors of thrombin.

Kolodziejczyk-Czepas et al. [64] further evaluated the effect of a bufadienolide-rich fraction from *K. daigremontiana* roots on the enzymatic properties of plasmin. They observed a 75% reduction in plasmin activity, with an IC_{50} of 16.70 μg/mL. The in silico analysis suggested that *K. daigremontiana* extracts contain compounds (bersaldegenin, bersaldegenin-1,3,5-orthoacetate, bersaldegenin-1-acetate, hovetrichoside C, and deigredorigenin-3-acetate) that may function as uncompetitive inhibitors of plasmin [64]. Additionally, in a previous study, it has been reported that the bufadienolide-rich fraction from *K.daigremontiana* roots did not induce cytotoxic effects to blood platelets at concentrations ranging from 1 to 50 μg/mL [27]. These results indicate that *K. daigremontiana* could be a valuable source of anti-thrombotic agents [45].

4.5. Hepatoprotective

The excessive accumulation of adipose tissue defines obesity. It serves as a primary risk factor for type 2 diabetes, a chronic disease with a complex etiology and significant socioeconomic and clinical implications, potentially affecting liver function. Considering the necessity for cost-effective therapeutic strategies, various plants, including *K. daigremontiana*, have gained recognition in traditional medicine. In this context, Madariaga-Navarrete et al. [19] investigated the effect of filtered juice from crushed leaves of *K. daigremontiana* (without the addition of any solvent) in a hyperglycemia-induced rat model, to support the antidiabetic application of *K. daigremontiana* in traditional medicine. The study found that the group fed a sugar-rich diet and supplemented with 2 mL of crude extract exhibited normal liver tissue architecture, similar to that of the positive control group. In contrast, the negative control group showed moderate liver damage. The authors attributed the beneficial effects of the crude extract to bioactive molecules; however, they did not characterize the extract's phytochemical profile. Although these results help validate the traditional use of *K. daigremontiana*, further robust studies are needed.

4.6. Antiaging and Skin Care

Skin aging is exacerbated by inflammatory processes driven by oxidative stress and external factors, including ultraviolet radiation, dietary habits, smoking, and psychological stress. Hering et al. [17] investigated the anti-aging properties of the extract obtained by crushing fresh leaves of *K. daigremontiana* in a transdermal diffusion skin model (Strat-M membrane), with pure water as a control. Their findings revealed the presence of

bufadienolides in the extract. Additionally, it was noted that after 24 h of diffusion through the skin model, no bufadienolide compounds were found in the subcutaneous filtrate, suggesting that these compounds cannot penetrate membranes. Nowak [65] formulated a topical product for human skin care incorporating *K. daigremontiana* extracts. This product has proven effective in treating skin conditions and disorders, including atopic dermatitis, psoriasis, allergic contact dermatitis, herpes virus infection, and acne. In this context, the application of *Kalanchoe daigremontiana* extracts in the development of skincare cosmetics or therapeutically effective topical treatments for specific medical skin disorders is promising. According to the authors, these effects were attributed to the bufadienolides and flavonoids present in *K. daigremontiana* extracts [17,65].

4.7. Cardiac Glycoside-like Effect

The pharmacological significance of bufadienolides lies in their potent cardiotonic properties. These compounds have potential therapeutic applications in the management of congestive heart failure and in regulating ventricular rate in supraventricular arrhythmias, owing to their ability to enhance myocardial contractility. As naturally occurring positive inotropic agents, they act through mechanisms analogous to those of traditional cardiac glycosides [45].

Scholtysik et al. [66] documented that a bufadienolide compound isolated by column chromatography (after Soxhlet extraction with methanolic and fractionation with butanol) from *K. daigremontiana* leaves exhibited cardiac glycoside-like effects (infused intravenously at a rate of 20 μg/kg/min) in a guinea pig model comparable to ouabain. However, at elevated doses (760–860 μg/kg/min), toxic effects were observed, resulting in ventricular arrhythmias and mortality. Nonetheless, n-butanol extracts from *Kalanchoe crenata* leaves have been reported to reduce blood pressure and heart rate in a normotensive anesthetized murine model of hypertension. The authors proposed that these extracts might exert cardiac effects by blocking potassium channels [67].

4.8. Cytotoxicity

The cytotoxic effects of *K. daigremontiana* have been examined using extracts from both leaves and roots. Research has primarily concentrated on aqueous, ethanolic, and methanolic extracts, as well as water and dichloromethane fractions. The extracts or fractions are typically concentrated to dryness or lyophilized, then resuspended in water and dimethyl sulfoxide prior to analysis. These extracts have been evaluated in vitro against a diverse array of human cancer cell lines, including ovarian (SKOV3), cervical adenocarcinoma (HeLa), breast (MCF-7), malignant melanoma (A375), liver (HepG2), lymphoblastic leukemia (H9 and J45.01), multiple myeloma (MM), mammary gland adenocarcinoma (MDA-MB 231), colon (HT29), Burkitt's lymphoma (Raji cells), as well as in blood platelets and human erythrocytes (Table 4).

Supratman et al. [68] isolated several bufadienolides from *K. daigemontiana* leaves and reported significant inhibitory activity against Epstein–Barr virus (EBV), which is closely linked to oncogenesis. Bryophillin A showed the highest potency, with an IC_{50} of 0.4 μM, whereas bryophilin C and bersaldegenin-3-acetate had IC_{50} values of 1.6 and 3.0 μM, respectively. Suppression of EBV activation was crucial for maintaining cell viability by preventing virus-induced transformation. Bryophillin A also demonstrated cytotoxicity against the A549 (human lung carcinoma) and HCT-8 (colon cancer) cell lines.

Table 4. Cytotoxic activity of *Kalanchoe daigremontiana*.

Plant Part	Extraction Method	Solvent	Resuspension/ Fractionation	Concentration	Model Assay	Relevant Results	Ref.
Leaves	Maceration (Extract was concentrated in a rotary evaporator, followed by fractionation)	Ethanol 95%	Aqueous and dichloromethane fractions were filtered, concentrated, and lyophilized prior to use	2–150 µg/mL	SKOV3 A375 HeLa S3 MCF-7	The dichloromethane fraction exhibited strong cytotoxicity (average IC_{50} 5.42 µg/mL) for all cell lines evaluated	[5]
Leaves	Maceration (Extracts were filtered, concentrated, and lyophilized)	95% Ethanol Water	The extracts were dissolved in DMSO and distilled water	0.1–150 µg/mL	SKOV-3 HeLa S3 MCF-7 A-375	Aqueous extract exhibited stronger cytotoxicity than ethanolic extract	[59]
Leaves	Maceration (Extract was filtered, concentrated, fractionated, and lyophilized)	95% Ethanol	Water and dichloromethane fractions were dissolved in DMSO	2–150 µg/mL	SKOV-3 HeLa S3 MCF-7 A-375	The dichloromethane fraction exhibited strong cytotoxicity across all cell lines (IC_{50} values < 10 µg/mL). Water fraction did not show cytotoxic effects	[13]
Leaves	Maceration (Extract was filtered, concentrated, and lyophilized)	Water	The dried extract was resuspended in distilled water	40–300 µg/mL	SKOV-3	Extract exhibited antiproliferative and cytotoxic activity	[21]
Leaves	Maceration	Ethanol	No information	3.9–500 µg/mL	HepG2	Extract showed strong antitumor activity (IC_{50}: 107.8 µg/mL)	[69]
Leaves	Maceration (Extract was concentrated in a rotary evaporator to dryness)	Ethanol 96%	No information	No information	J45.01H9 cells	Ethanolic extract exhibited cytotoxicity against H9 cells (IC_{50}: 359.4 µg/mL)	[11]
Leaves	Maceration	Water	Not used	1.57 mg/mL	MM cells	The extract showed moderate cytotoxicity	[24]

Table 4. *Cont.*

Plant Part	Extraction Method	Solvent	Resuspension/ Fractionation	Concentration	Model Assay	Relevant Results	Ref.
Leaves	Leaching (Extract was filtered and concentrated in a rotary evaporator)	EthanolWater: 95%:	The concentrated extract was used for the preparation of phytosomes	1–100 µg/mL	MCF-7 HeLa	Phytoniosomes showed cytotoxicity at 25 µg/mL in both cell lines	[28]
Leaves	Maceration (Extract was concentrated using a rotary evaporator)	Methanol 100%	Extract was resuspended at 1 mg/mL in 0.5% (*w*/*v*) DMSO	500–1000 µg/mL	human blood erythrocytes	The extract showed cytotoxicity against human erythrocytes in a dose-dependent response	[54]
Leaves	Leaching (Extract was concentrated in a rotary evaporator to dryness)	Ethanol water: 1:2 (*v*/*v*):	No information	25–200 µg/mL	MDA-MB-231 metastatic breast cancer	Encapsulated extract showed a higher cytotoxic effect (IC_{50} 48.53 µg/mL) than the non-encapsulated extract (IC_{50} 61.29 µg/mL)	[48]
Leaves	Maceration (Extract was concentrated in a rotary evaporator)	Methanol 100%	No information	No information	Raji cells	Extract exhibited potent inhibitory effects on Epstein–Barr virus early antigen activation	[68]
Leaves	Ultrasonic waves(Aqueous extract was freeze-dried. Ethanolic extract was evaporated in a hot-air oven to dryness)	WaterEthanol	No information	5–70 µg/mL	HT29 human colon cancer	Aqueous and ethanolic extracts showed antiproliferative properties (IC_{50}: 42.81 µg/mL)	[55]
Roots	Maceration (Extract was concentrated in a rotary evaporator and lyophilized).	Water	Dried extract was suspended in 1% (*v*/*v*) aqueous methanol to obtain a bufadienolide-rich fraction	1–50 µg/mL	Blood platelets	The bufadienolide-rich fraction did not induce damage to blood platelets	[27]

DMSO: dimethyl sulfoxide; SKOV3: Sloan-Kettering Ovarian Cancer Cell Line 3; HeLa: cervical adenocarcinoma, MCF-7: breast cancer cell line; A375: malignant melanoma cell line, HepG2: human liver cancer cell line; H9 and J45.01: lymphoblastic leukemia cell lines, MM: multiple myeloma cells, MDA-MB 231: mammary gland adenocarcinoma cell line, HT29: adenocarcinoma colon cell line, Raji cells: Burkitt's lymphoma.

Stefanowicz-Hajduk et al. [5] studied the effects of *K. daigremontiana* leaf water and dichloromethane fractions on SKOV-3, HeLa, MCF-7, and A375 human cancer cell lines. The water fraction did not exhibit cytotoxicity, with a half-maximal inhibitory concentration (IC_{50}) higher than 100 µg/mL, whereas the dichloromethane fraction was strongly cytotoxic across all lines (IC_{50} 5.42–8.02 µg/mL). Earlier research found that aqueous *K. daigremontiana* leaf extracts were cytotoxic to HeLa (IC_{50} 1.48 µg/mL), SKOV-3 (IC_{50} 10.12 µg/mL), and A375 (IC_{50} 36.05 µg/mL), while ethanolic extracts were not (IC_{50} > 100 µg/mL) [59]. Another study reported that both aqueous and ethanolic extracts were not cytotoxic to these cell lines. Still, the dichloromethane fraction was highly cytotoxic (IC_{50} < 10 µg/mL), possibly because of bersaldegenin-1,3,5-orthoacetate [13]. In 2022, the same researchers showed that 200 µg/mL of the *K. daigremontiana* leaf water fraction lowered SKOV-3 cell viability to 38.3%, with a cell death rate of 39.85% [21]. The cytotoxic effects of *K. daigremontiana* bioactive compounds are usually attributed to their ability to block the cell cycle at the S and G2/M phases. This leads to apoptosis through mitochondrial dysfunction, which releases pro-apoptotic factors and activates the caspase cascade. When the mitochondrial membrane loses integrity, likely due to reactive oxygen species, it triggers mitochondrial permeability changes, leading to irreversible DNA fragmentation and cell death, as a result of the combined action of phenolic acids, flavonoids, and bufadienolides [21,59].

Bogucka-Kocka et al. [11] found that ethanolic extracts from *K. daigremontiana* leaves, prepared by accelerated solid extraction and maceration, showed low cytotoxicity in H9 (human T-cell) and J45.01 (human acute lymphoblastic leukemia) cell lines, with IC50 values of 844/956 and 712/359 µg/mL, respectively. The extraction method affected cytotoxicity, which was linked to the specific compounds isolated. Similarly, Pestana et al. [69] evaluated the cytotoxic activity of aqueous and ethanolic *K. daigremontiana* leaf extracts against hepatocellular carcinoma (HepG2) cells. The ethanolic extract was more cytotoxic (IC_{50} 107.8 µg/mL) than the aqueous extract (IC_{50}: 279.5 µg/mL). At the same time, both solvents extracted similar compounds; ethanol improved compound recovery and increased cytotoxic potency against HepG2 cells. Additionally, the aqueous extract of *K. daigremontiana* leaves reduced the viability of multiple myeloma cells (MM-RPMI 8226 line) to 47.8% at 1.57 mg/mL. This effect was attributed to the inhibition of mitochondrial NADH dehydrogenase activity, which decreased cell viability. The extract also caused a 19% reduction in mitochondrial membrane potential, leading to oxidative stress and the oxidation of cancer cells [24].

Vergara-Castañeda et al. [55] demonstrated that the ethanolic extract exhibited the highest inhibition of cell proliferation (67.10%) at 71.42 µg/mL, whereas the aqueous extract produced a lower, dose-dependent inhibition (45.04%). The antiproliferative activity was associated with the presence and concentration of specific phytochemicals. Alvarado-Palacios et al. [48] formulated a nanoencapsulated *K. daigremontiana* leaf extract and assessed its efficacy against metastatic breast cancer (MDA-MB-231) and non-cancerous breast cells (MCF 10A). The nanoencapsulated extract was more effective than the free extract in inhibiting MDA-MB-231 cells, with IC_{50} values of 48.53 µg/mL and 61.29 µg/mL, respectively. Notably, the nanoencapsulated treatment did not induce cytotoxicity in healthy MCF-10A cells, even at 200 µg/mL, whereas the free extract exhibited significant toxicity, with an IC_{50} of 100.2 µg/mL. The observed cytotoxicity was attributed to apoptosis, as evidenced by nuclear fragmentation, chromatin condensation, organelle degradation, and cell membrane deformation.

A recent study investigated *K. daigremontiana*-loaded phytoniosomes to enhance the anticancer efficacy of radiotherapy in HeLa and MCF-7 cell lines. Short-term exposure (24 h) demonstrated comparable activity between the free extract and the encapsulated form. In contrast, long-term exposure (72 h) to 100 µg/mL of phytoniosomes resulted in

significant cell death. Combining radiotherapy with a minimal dose of phytoniosomes (1 μg/mL) was highly effective, reducing cell viability to approximately 7% in MCF-7 and 8% in HeLa cells. These findings suggest that the *K. daigremontiana* extract functions as a radiosensitizer by disrupting mitochondrial membrane potential and augmenting radiation-induced pro-apoptotic effects [28]. Elizondo-Luévano et al. [54] further reported that methanolic *K. daigremontiana* leaf extract exhibited low cytotoxicity on human erythrocytes, with 7.4% hemolysis observed in a concentration-dependent manner. No toxic effects were detected at concentrations below 0.2 mg/mL. Additionally, a bufadienolide-rich fraction from *K. daigremontiana* roots did not exhibit cytotoxicity in blood plasma at concentrations ranging from 1 to 50 μg/mL, likely due to the potent antioxidant properties of *K. daigremontiana* extracts [27].

Current evidence indicates that extracts or fractions from *K. daigremontiana* leaves and roots exhibit significant in vitro cytotoxicity, supporting their traditional use in cancer therapy. However, additional studies are necessary to assess the in vivo cytotoxic, antiproliferative, and antitumor effects of *K. daigremontiana*.

4.9. Other Research Uses of Plant Parts, Pulp, Extracts, and Isolated Compounds from Kalanchoe daigremontiana

Additional applications of *K. daigremontiana* extracts or plant parts have been documented, including their use to treat scabies in rabbits [70], their performance in goats, laying hens, and broiler chickens [31,71,72], and their use as insecticides [38,73]. Moreover, extracts from *K. daigremontiana* have been employed as reducing agents in the green synthesis of nanoparticles for diverse applications [55,74,75].

In a recent study, Sifuentes-Saucedo et al. [70] developed an oleate derived from *K. daigremontiana*, using olive oil as a base, for the treatment of scabies in rabbits. The treatment regimen involved applying oleate to the rabbits' ears and legs over four days, resulting in the complete eradication of scabies and the healing of the rabbits' ears and legs. The efficacy of the oleate may be attributed to the presence of secondary metabolites, flavonoids, and terpenes in *K. daigremontiana*.

Vázquez-García et al. [71] investigated the impact of *K. daigremontiana* supplementation over a 52-day period (2 kg of dried plant per ton of feed) on renal and hepatic functions, metabolic processes, and reproductive performance (including weight changes and reproductive efficiency) in multiparous Alpine goats during the breeding season. The findings indicated that moderate inclusion of *K. daigremontiana* did not affect renal function, as evidenced by the absence of significant differences in blood urea nitrogen and creatinine levels between the control and supplemented groups at the end of the bioassay. Similarly, hepatic function remained unaffected, with no significant variations in alanine aminotransferase and gamma-glutamyl transpeptidase activities among the groups and inconsistent values for alkaline phosphatase, aspartate aminotransferase, and albumin across sampling dates, suggesting no discernible impact on liver function. Additionally, there were no significant changes in metabolic markers (glucose and cholesterol), nor were there differences in body weight and reproductive performance across treatments. Notably, the supplemented group exhibited an earlier conception date than the control group. The authors emphasized the need for further research to ascertain the optimal supplementation level that enhances productivity and reproductive benefits while mitigating potential toxicity.

Korczyński et al. [31] investigated the potential use of *the K. daigremontiana* plant as a feed additive for increasing the productivity of laying hens. They evaluated the impact of incorporating 5% of pulp from *K. daigremontiana* into the diet of laying hens over a 45-week period. The study revealed that this dietary modification did not influence the hens' performance or their biochemical blood parameters. Additionally, the inclusion of the pulp did not affect eggshell strength, yolk color, or egg protein quality. However, it was

observed that eggs from hens receiving the pulp supplementation were heavier compared to those from the control group. Blood analyses indicated comparable levels of aspartate aminotransferase and alkaline phosphatase between the two groups, although alanine aminotransferase levels were elevated in the pulp-supplemented group. By the conclusion of the study, the group receiving the pulp exhibited a 15% reduction in total cholesterol levels. Initially, antioxidant activity, as measured by glutathione peroxidase, was higher in the pulp-supplemented group, but this difference was not sustained by the end of the experiment. The authors concluded that *K. daigremontiana* did not enhance egg quality or hen health and was deemed unsuitable as a feed additive. On the other hand, recently it has been reported that the incorporation of *K. daigremontiana* dried plant (20 g/ton of basal diet) on broiler chicken diet over 49 days significantly improves productive performance (daily weight gain, final weight, better feed conversion) and liver indicators (lower concentrations of liver enzymes and troponin T) in broiler chickens [72].

Insecticidal compounds play a crucial role in agricultural practices, as they are essential for managing insect pests. In this regard, *K. daigremontiana* has been documented to possess insecticidal properties against third-instar larvae of silkworms, with particular emphasis on bufadienolides isolated from the ethyl acetate fraction of its leaves. These effects are primarily attributed to the structural characteristics of these compounds, notably the presence of oxygenated substituents (at C-11 and C-12) on the C-ring [38,73].

Furthermore, *K. daigremontiana* leaf extracts have been effectively utilized as reducing agents in the eco-friendly synthesis of inorganic nanoparticles for various applications. Morales et al. [76] successfully synthesized magnetic nanoparticles for mercury removal in aqueous media, using ferric chloride hexahydrate and ferrous chloride tetrahydrate as precursors, with *K. daigremontiana* leaf extracts serving as the reducing agent, achieving a mercury removal efficiency exceeding 75% in aqueous solutions. Additionally, silver nanoparticles (AgNPs), which exhibit photocatalytic activity against methylene blue and antimicrobial properties against *Escherichia coli* and *Staphylococcus aureus*, have been synthesized using *K. daigremontiana* leaf extracts as a stabilizing agent and silver nitrate as a precursor [74]. Moreover, AgNPs synthesized with *K. daigremontiana* leaf extract demonstrated stability for up to 27 months under dark conditions without significant alterations in their physical properties [75]. Vergara-Castañeda et al. [55] synthesized gold nanoparticles using a gold(III) chloride solution as a precursor and *K. daigremontiana* leaf extract as a reducing agent. These nanoparticles exhibited antiradical and reducing properties in the ORAC and ABTS assays, as well as the ability to inhibit HT29 cancer cell growth and modulate cellular peroxides, indicating their potential use in biomedical and pharmaceutical fields. Authors agree that the phytochemical profile of *K. daigremontiana* leaf extracts significantly impacts the properties of synthesized nanoparticles.

5. Toxicological Reports of *Kalanchoe daigremontiana*

While *K. daigremontiana* is traditionally acknowledged for its medicinal properties in addressing various ailments, caution is warranted regarding its use and consumption in forms such as salads, juices (fresh extracts obtained after crushing leaves), infusions, and decoctions [3]. This caution is necessitated by the presence of compounds, specifically glycosidic aglycones and steroids, which are toxic to the human body at higher doses [15]. It is noteworthy that *K. daigremontiana* is classified as a toxic plant (like other *Kalanchoe* species [5]) in some countries, including Mexico, South Africa, and Australia [8,71].

It has been indicated that *K. daigremontiana* plants contain compounds (cardiac glycosides) toxic to wildlife [7]. Nonetheless, this plant could be toxic to cattle and other farm animals when consumed without adequate forage [5,71]. Moreover, previous studies have documented toxic effects, including depression, muscular incoordination, twitching, neck

spiraling, tremors, convulsions, paralysis, and death, in 2-week-old chicks that ingested between 0.8% and 1.2% of their body weight in *K. daigremontiana* leaves [77]. Additionally, it has been reported that the A2 compound isolated from *K. daigremontiana* leaves elicits typical electrocardiogram (ECG) signs of digitalis intoxication when administered intravenously to guinea pigs, leading to ventricular arrhythmias at 760 μg/kg and death at 860 μg/kg.

In the *Artemia salina* model, it has been documented that the lethal dose of *K. daigremontiana* extracts depends on the solvent used. The n-hexane soluble partitionate exhibited an LC_{50} value of 70.71 μg/mL, followed by the methanol extract with an LC_{50} of 59.46 μg/mL, the chloroform soluble partitionate with a median lethal concentration (LC_{50}) of 4.42 μg/mL, and the carbon tetrachloride soluble partitionate with an LC_{50} of 0.78 μg/mL. According to Clarkson's index, these extracts are classified as toxic to humans (LC_{50} < 100 μg/mL), yet they may have potential as chemoprotective agents [78].

In contrast, no toxicological effects were observed in goats when a moderate inclusion of *K. daigremontiana* leaves (2 kg/ton of feed) was assessed [71]. Similarly, no adverse effects were noted in laying hens (5% of pulp from *K. daigremontiana* in the basal diet) [33] and broiler chickens (20 g/ton of basal diet) [72]. Furthermore, the methanolic extract from *K. daigremontiana* leaves demonstrated low toxicity in human erythrocytes, with erythrocyte hemolysis of less than 0.5% at 100 μg/mL and 7.4% at 1000 μg/mL [16]. Consistent findings were reported by Elizondo-Lluevano et al. [54] who observed no toxicity in human erythrocytes at concentrations below 0.2 mg/mL.

One potential approach to mitigate the toxicity of *K. daigremontiana* extracts or isolated compounds is to formulate modified liposomes or nanocapsules. Alvarado-Palacios et al. [48] successfully nanoencapsulated a hydroalcoholic extract derived from *K. daigremontiana* leaves, demonstrating an absence of cytotoxic effects on normal cells at 200 μg/mL, while exhibiting selective effects on breast cancer cell lines.

Given the limited information on the toxicological potential of *Kalanchoe daigremontiana*, some phytochemicals identified in *K. daigremontiana* were selected for in silico analysis to further elucidate their physicochemical, drug-likeness, and toxicity through SwissADME database (https://www.molecular-modelling.ch/swiss-drug-design.html; accessed on 10 March 2026), absorption was analyzed on pkCSM server (https://biosig.lab.uq.edu.au/pkcsm/prediction; accessed on 10 March 2026), and toxicological properties were tested on ProTox 3.0 platform (https://tox.charite.de/protox3/index.php?site=compound_input; accessed on 10 March 2026) and ADMET-AI server (https://admet.ai.greenstonebio.com/; accessed on 10 March 2026). In addition, SMILES nomenclature for each compound was obtained from the PubChem database (https://pubchem.ncbi.nlm.nih.gov/; accessed on 10 March 2026).

Figure 2 illustrates radar plots depicting the principal physicochemical properties of nine compounds derived from *K. daigremontiana*, including gallic acid, kaempferol, quercetin, bufadienolide, daigremontianin, bryophyllin A, bryophyllin B, bryophyllin C, and bersaldegenin. These plots assess parameters such as molecular size (SIZE), insolubility (INSOLU), flexibility (FLEX), lipophilicity (LIPO), polarity (POL), and unsaturation (INSATU), which collectively characterize the oral bioavailability and drug-likeness of these compounds. The radar plot profiles for gallic acid, kaempferol, and quercetin predominantly remained within the pink area, except for unsaturation, indicating the optimal range for oral drug absorption. This observation suggests that these molecules exhibit a balanced profile of hydrophobicity and molecular weight, which facilitates their passive diffusion across biological membranes [79].

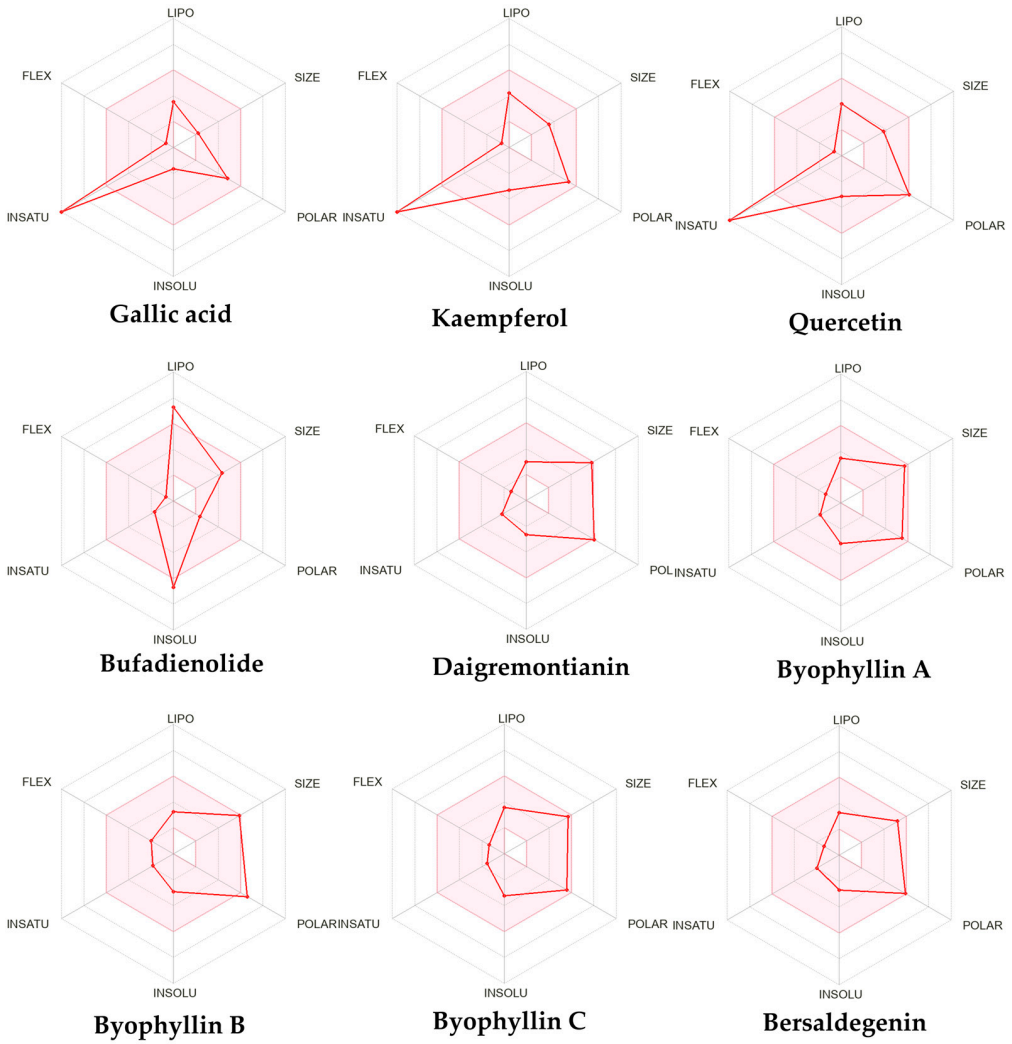


Figure 2. Physicochemical properties assessed for *Kalanchoe daigremontiana* compounds include lipophilicity (LIPO), molecular size (SIZE), polarity (POLAR), insolubility (INSOLU), unsaturation (INSATU), and flexibility (FLEX). The pink shaded region shows the suitable physicochemical range that the radar plot of the target compound must entirely encompass to be considered drug-like. The red line shows the physicochemical properties of the corresponding compound.

Conversely, the radar plots for daigremontianin, byophyllin A, byophyllin B, byophyllin C, and bersaldegenin revealed deviations along the saturation and polarity axes. These deviations suggest a more intricate molecular architecture. The reduced saturation values of these compounds indicate a rigid, polycyclic steroidal framework that, while enhancing molecular recognition and binding affinity for specific biological targets, may limit metabolic flexibility. Additionally, the shifts in polarity imply a more specialized permeation profile than that of highly compliant phenolic compounds. Bufadienolide demonstrates increased lipophilicity, suggesting a propensity to associate with lipid environments and potentially traverse cell membranes [79].

These diverse physicochemical characteristics suggest that *K. daigremontiana* metabolites exhibit structural diversity, which could lead to varied interactions with target proteins and diverse biological effects.

Figure 3 presents a "boiled egg plot" that illustrates the relationship between lipophilicity (WLOGP, Y-axis) and polarity (TPSA, X-axis) for the nine compounds derived from *K. daigremontiana*. This plot serves as a predictive tool for assessing a compound's potential to traverse biological barriers, such as the blood–brain barrier (BBB, yellow region) and

human intestinal absorption (HIA, white region). All compounds, except for byophyllin B, are located within the white region, indicating highly probable human intestinal absorption. Byophyllin B, however, is situated outside both regions, suggesting limited absorption and poor barrier permeability [79].

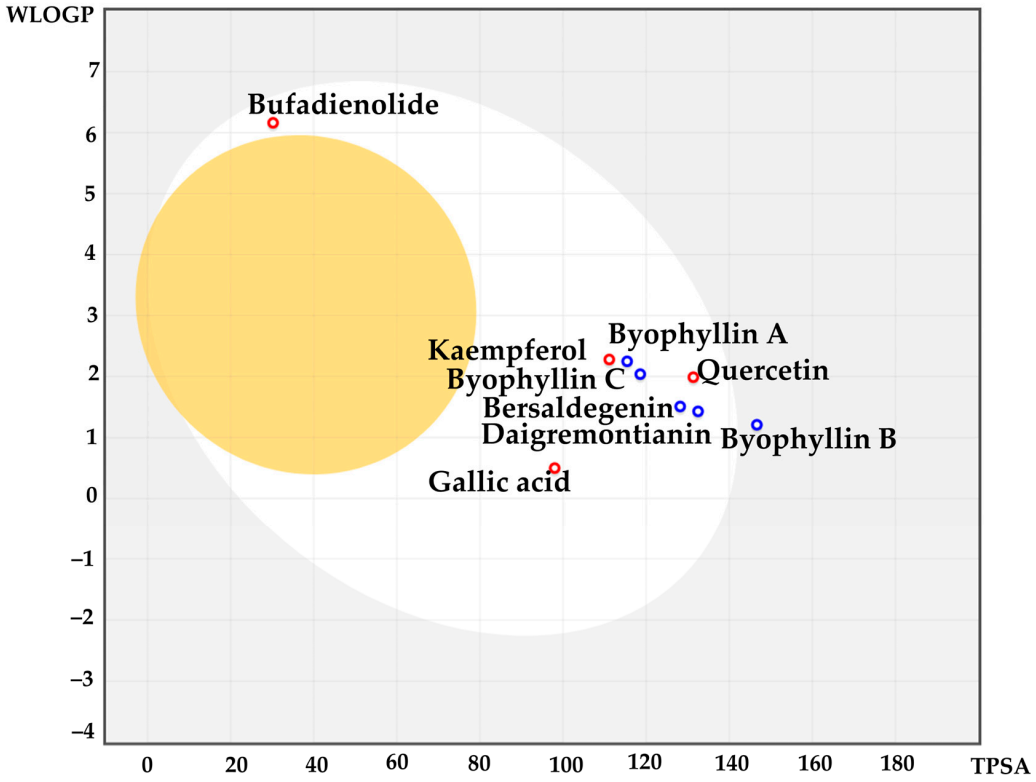


Figure 3. Egg plot from SwissADME exhibits the water partition coefficient (WlogP) versus the topological polar surface area (TPSA) for *Kalanchoe daigremontiana* compounds. Propensity of compounds to be substrate of P-gp by coloured points: blue for substrate (PGP+) and red for non-substrate (PGP−) [79].

The in silico toxicological properties of the compounds selected from *K. daigremontiana* are presented in Table 5. The pharmacological characteristics of a molecule can be assessed using the Lipinski, Ghose, Veber, Egan, and Muegge filters or rules. Lipinski's rules evaluate properties such as molecular weight (MW < 500 g/mol), the number of hydrogen-bond donors (HBD < 5), the number of hydrogen-bond acceptors (HBA < 10), and lipophilicity (LogP > 5). Ghose's rules are based on molecular weight (160 g/mol > MW < 480 g/mol), lipophilicity (−0.4 > LogP < 5.6), molar refractivity (40 < MR < 130), and the number of atoms (20 < nA < 70). Veber's rules consider parameters such as rotatable bonds (RB < 10) and polar surface area (PSA < 140 Å). Egan's rules propose filters based on molecular weight (500 g/mol > MW), lipophilicity (−0.4 < LogP < 5), and the number of hydrogen bond acceptors (HBA < 10). Finally, the Muegge filters focus on molecular weight (200 g/mol > PM < 600 g/mol), the number of hydrogen bond donors (nEDH < 5), the number of hydrogen bond acceptors (nEAH < 10), lipophilicity (−2 < LogP < 5), and structural features [79]. Based on this analysis, kaempferol, quercetin, bryophillin A, bryophillin C, and bersaldegenin were the only compounds that did not violate any of the aforementioned rules. In contrast, bufadienolide was identified as the compound with the most violations across different rules, including those of Lipinski, Ghose, Egan, and Muegge.

Table 5. In silico toxicological properties of compounds from *Kalanchoe daigremontiana*.

Prediction Platform	Formula	$C_7H_6O_5$	$C_{15}H_{10}O_6$	$C_{15}H_{10}O_7$	$C_{24}H_{34}O_2$	$C_{26}H_{30}O_9$	$C_{26}H_{32}O_8$	$C_{26}H_{34}O_9$	$C_{26}H_{34}O_8$	$C_{24}H_{32}O_7$
	Compound	**Gallic Acid**	**Kaempferol**	**Quercetin**	**Bufadienolide**	**Daigremontianin**	**Bryophyllin A**	**Bryophyllin B**	**Bryophyllin C**	**Bersaldegenin**
SwissADME	**Drug likeness and bioavailability**									
	* Lipinski	Yes, 0	Yes, 0	Yes, 0	Yes, 1	Yes, 0	Yes, 0	Yes, 0	Yes, 0	Yes, 0
	* Ghose	No, 2	Yes	Yes	No, 1	No, 1	Yes	No, 1	Yes	Yes
	* Veber	Yes	Yes	Yes	Yes	Yes	Yes	No, 1	Yes	Yes
	* Egan	Yes	Yes	Yes	No, 1	No, 1	Yes	No, 1	Yes	Yes
	* Muegge	No, 1	Yes	Yes	No, 1	Yes	Yes	Yes	Yes	Yes
	[1] Bioavailability score	0.56	0.55	0.55	0.55	0.55	0.55	0.55	0.55	0.55
pkCSM	**Absorption**									
	[2] Water solubility	−2.56	−3.04	−2.925	−5.567	−3.88	−4.113	−3.58	−3.896	−3.916
	[3] Caco-2 permeability	−0.081	0.032	−0.229	1.223	1.176	1.351	0.57	1.202	0.411
	[4] Intestinal absorption	43.374	74.29	77.207	99.54	100	85.237	92.164	80.023	73.917
	[5] Skin Permeability	−2.375	−2.735	−2.735	−2.669	−2.964	−2.977	−2.788	−2.91	−3.154
	[6] P-glycoprotein substrate	No	Yes	Yes	No	Yes	No	Yes	Yes	Yes
	[7] P-glycoprotein I inhibitor	No	No	No	Yes	No	No	No	No	No
	Toxicity parameters									
	[8] AMES toxicity	No	No	No	No	No	No	No	No	No
	[9] Max. tolerated dose	0.7	0.531	0.499	−0.206	−1.179	−1.3	−1.106	−1.213	−0.722
	[10] hERG I inhibitor	No	No	No	No	No	No	No	No	No

Table 5. *Cont.*

Prediction Platform	Formula	$C_7H_6O_5$	$C_{15}H_{10}O_6$	$C_{15}H_{10}O_7$	$C_{24}H_{34}O_2$	$C_{26}H_{30}O_9$	$C_{26}H_{32}O_8$	$C_{26}H_{34}O_9$	$C_{26}H_{34}O_8$	$C_{24}H_{32}O_7$
	Compound	**Gallic Acid**	**Kaempferol**	**Quercetin**	**Bufadienolide**	**Daigremontianin**	**Bryophyllin A**	**Bryophyllin B**	**Bryophyllin C**	**Bersaldegenin**
	[11] hERG II inhibitor	No	No	No	Yes	No	No	No	No	No
	[12] Oral Rat Acute Toxicity (LD50)	2.218	2.449	2.471	2.618	3.025	2.337	2.431	2.706	2.241
	[13] Oral Rat Chronic Toxicity (LOAEL)	3.06	2.505	2.612	0.819	2.4212	1.636	2.144	1.818	1.932
	[14] Hepatotoxicity	No	No	No	No	Yes	Yes	Yes	No	Yes
	[15] *T.Pyriformis* toxicity	0.285	0.312	0.288	0.36	0.285	0.286	0.285	0.285	0.292
ProTox 3.0	**Toxicity parameters**									
	[16] LD_{50} (Human)	2000	3919	159	25	Compound nor found	Compound nor found	Compound nor found	Compound nor found	25
	[17] Toxicity class	4	5	3	2	Compound nor found	Compound nor found	Compound nor found	Compound nor found	2
ADMET-AI	[18] Clinical Toxicity	0.03	0.03	0.03	0.04	0.10	0.12	0.13	0.17	0.08
	[19] Mutagenicity	0.15	0.41	0.56	0.06	0.28	0.45	0.11	0.31	0.08
	[20] Drug-Induced Liver Injury	0.71	0.90	0.93	0.20	0.62	0.36	0.17	0.27	0.15
	[21] Carcinogenicity	0.10	0.03	0.03	0.12	0.02	0.01	4.22×10^{-3}	0.01	0.01

* Yes/No, number of violations of Lipinski, Ghose, Veber, Egan, and Muegge rules; [1] Probability score; [2] Water solubility (log mol/L); [3] Caco2 permeability (log Papp in 10^{-6} cm/s); [4] Intestinal absorption (human) (% absorbed); [5] Skin Permeability (log Kp); [6] P-glycoprotein substrate (Yes/No); [7] P-glycoprotein I inhibitor (Yes/No); [8] AMES toxicity (Yes/No); [9] Max. tolerated dose (human) (log mg/kg/day); [10] hERG I inhibitor (Yes/No); [11] hERG II inhibitor (Yes/No); [12] Oral Rat Acute Toxicity (LD_{50}) (mol/kg); [13] Oral Rat Chronic Toxicity (LOAEL) (log mg/kg bw/day); [14] Hepatotoxicity (Yes/No); [15] *T.Pyriformis* toxicity (log ug/L); [16] LD_{50} (Human) (mg/kg); [17] Toxicity class is in the classification form 1 to 6. Class 1 is the most toxic and lethal, and class 6 is non–toxic. [18] Clinical Toxicity (probability score); [19] Mutagenicity (probability score); [20] Drug-Induced Liver Injury (probability score); [21] Carcinogenicity (probability score).

To enhance understanding of a compound's bioavailability, several factors were evaluated, including water solubility, Caco-2 permeability, intestinal absorption, skin permeability, and the compound's role as a substrate or inhibitor of P-glycoprotein. Among the compounds analyzed, gallic acid exhibited superior water solubility, whereas bryophyllin A demonstrated the highest permeability across Caco-2 cell membranes. Furthermore, daigremontianin and gallic acid were identified as having optimal intestinal absorption and skin permeability, respectively. Kaempferol, quercetin, daigremontianin, bryophyllin B, and bryophyllin C functioned as substrates of P-glycoprotein, which is known to decrease intracellular compound accumulation. Conversely, bufadienolide was identified as an inhibitor of this protein, indicating its potential to enhance the intracellular concentration and bioavailability of drugs. However, this effect may also be detrimental, as it could increase the toxicity of co-administered drugs [80].

Three distinct platforms, including pkCSM [80], ProTox 3.0 [81], and ADMET-AI [82], were utilized to evaluate the toxicity parameters of the nine compounds selected from *K. daigremontiana*. These parameters encompassed the median lethal dose (LD_{50}) in both human and murine models, toxicity classification, and specific toxicity types, including mutagenicity, carcinogenicity, and hepatotoxicity. The analyzed compounds exhibited a spectrum of toxicities, ranging from class 5 (low toxicity) to class 2 (toxic). For example, quercetin, gallic acid, and kaempferol demonstrated LD_{50} values of 159, 2000, and 3919 mg/kg, respectively, corresponding to classes 3, 4, and 5, indicating a low toxicity risk. In contrast, compounds such as bufadienolide and bersaldegenin presented LD_{50} values of 25 mg/kg, classified as class 2, suggesting high toxicity. Conversely, daigremontianin, bryophyllin A, bryophyllin B, and bryophyllin C were not found on the ProTox 3.0 server [81].

Regarding the maximum tolerated daily dose, gallic acid exhibited a more favorable response than all other compounds, whereas bryophyllin C was the least benign. Among other parameters related to optimal compound doses, acute and chronic oral toxicity in rats were considered, with gallic acid and bufadienolide showing the lowest optimal values in these categories. Additionally, daigremontianin, bryophyllin A, bryophyllin B, and bersaldegeninan were found to be potentially hepatotoxic. Conversely, the ADMET-AI platform predicted a high propensity for quercetin to cause liver damage (0.93) and to be mutagenic [82]. Bufadienolide emerged as the compound with the greatest potential to induce toxicity in the aquatic model *Tetrahymena pyriformis*, exhibited the highest value among the compounds for cancer induction, and was the sole compound to inhibit hERG II, a property associated with cardiac toxicity. Other parameters, such as hERG I inhibition and the AMES mutagenicity test, indicated that all compounds presented minimal risk on these indicators [80].

6. Regulatory and Commercialization Challenges for *K. daigremontiana*

Traditional medicine often uses herbal remedies, preparing infusions, decoctions, and extracts from whole plants or specific parts to treat various ailments. About 80% of the global population relies on herbal formulations for primary healthcare, driven by cultural practices and affordability, and this trend is growing. *K. daigremontiana* is recognized for its medicinal properties and is used to treat health conditions in Mexico, the USA, Brazil, Peru, South Africa, India, and Poland [5,8]. However, its transition from traditional use to global acceptance as a modern medicine faces significant safety and regulatory challenges [83,84].

In Mexico, the General Health Law recognizes herbal medicines; however, there is a significant regulatory gap for species such as *Kalanchoe*, which are frequently marketed as dietary supplements or herbal remedies. As a result, these products are not required to demonstrate quality, potency, or safety prior to market entry. Many herbal medicines remain unregistered and are distributed without essential safety or toxicological assessments.

For instance, a range of *K. daigremontiana*-based products, including capsules, powders, dried leaves, and concentrated extracts, is available online as dietary supplements. Some are labeled "natural 100% natural," and their recommended uses are based on traditional practices and ancestral knowledge. These products claim to support schizophrenia treatment, promote healing, reduce inflammation, combat cancer or cellular damage, aid in hypertension, and relieve pain. Nevertheless, these claims lack scientific or clinical support.

In this context, adverse effects associated with herbal remedies frequently result from misidentification of plants, adulteration, undeclared substances, contamination, incorrect dosing, and consumer misuse [85]. To mitigate these risks, protocols should be implemented to validate the therapeutic use of *K. daigremontiana* and standardize its formulations. This process should include comprehensive pharmacokinetic and pharmacodynamic characterization to facilitate integration into regulated pharmacological practices in Mexico and internationally. Strengthening legislative frameworks through collaboration among research centers, universities, and government agencies is essential to ensure scientific validation, standardization, and effective regulation of the commercialization of *K. daigremontiana* [83,84].

7. Conclusions

Kalanchoe daigremontiana is extensively utilized in traditional medicine as an alternative remedy for various ailments, including burns, rheumatic conditions, hypertension, diabetes, renal pain, diarrhea, microbial infections, cough, fever, deep wounds, gangrene, ulcers, skin irritation, gastric issues, asthma, abscesses, anxiety, inflammation, and cancer. Leaves are predominantly used to prepare infusions, decoctions, cataplasms, macerated extracts, and fresh extracts obtained after crushing leaves.

A wide array of phytochemicals, chiefly phenolic compounds and bufadienolides, have been identified in this plant species. These phytochemicals exhibit a range of bioactivities, including antioxidant, antibacterial, antifungal, antiviral, antiparasitic, anthelmintic, anti-inflammatory, anticoagulant, anti-aging, dermatological, cytotoxic, antitumoral, antiproliferative, hepatoprotective, and cardiac glycoside-like effects.

Crude extracts and bufadienolide-rich fractions have demonstrated toxic effects in 2-week-old chicks, guinea pigs, and *Artemia salina*. However, no toxicity has been reported in goats, broiler chickens, laying hens, or human erythrocytes. Although *K. daigremontiana*-based products are commercially available as dietary supplements with various health claims, they lack scientific validation. Consequently, further research is necessary to ascertain the level of human exposure to traditional and commercial products. Given the absence of clinical studies providing guideline values for toxicity and the lack of scientific data to ensure safety, extreme caution should be exercised.

Despite the potential pharmaceutical applications of *K. daigremontiana*, further research is imperative to elucidate its effects, dosage, mechanisms, long-term safety, and side effects. Clinical studies are essential to validate its therapeutic potential and determine the concentration limits for beneficial effects and toxic thresholds of this species. Until such data becomes available, the cautious use and consumption of *K. daigremontiana* are recommended.

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