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Review Paper

A Comprehensive Review on Kalanchoe tomentosa

Prachi Gupta*, J. V. Vyas, Dr. Vivek Paithankar, Dr. Anjali Wankhade

Department of Pharmacology, Vidhyabharati College of Pharmacy, Amravati.

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ABSTRACT

Kalanchoe tomentosa (Crassulaceae), commonly known as the Panda Plant, is a perennial succulent native to Madagascar and widely recognized for both its ornamental and medicinal value. The plant contains various biologically active secondary metabolites, including flavonoids, triterpenoids, bufadienolides, phenolic compounds, and sterols, which are responsible for its diverse pharmacological properties. Ethnobotanical and scientific studies have reported its antioxidant, anti-inflammatory, antimicrobial, antidiabetic, antileishmanial, wound-healing, and cytotoxic activities. Phytochemical analyses reveal compounds such as α-amyrin acetate, β-sitosterol, quercetin, and gallic acid, contributing to its bioactivity. Extraction methods using solvents of varying polarities (hexane, chloroform, methanol) have been optimized for isolating these metabolites. Despite promising biological effects, research on K. tomentosa remains largely preclinical, with limited data on its pharmacokinetics, molecular mechanisms, and safety profile. This review highlights the botanical features, traditional uses, phytochemistry, pharmacological activities, and future research directions of K. tomentosa, emphasizing its potential as a source of novel therapeutic agents for oxidative stress, inflammation, diabetes, and cancer management..

INTRODUCTION

Kalanchoe tomentosa, belonging to the family Crassulaceae, is a perennial, succulent plant characterized by its dense covering of white, hair-like structures. Commonly known as the Panda Plant, it is native to Madagascar. The genus Kalanchoe comprises approximately 130 species of annual and perennial herbs, shrubs, climbers, and small trees. These species are typically found in semi-desert or shaded regions of Saudi Arabia, Yemen, Central Africa, Madagascar, Asia, Australia, and tropical America. The plant is often cultivated as an ornamental species in rock and sand gardens under moderate humidity conditions. Beyond its ornamental importance, Kalanchoe tomentosa is recognized for its medicinal properties, exhibiting antimicrobial, anti-

***Corresponding Author:** Prachi Gupta
Address: *Vidhyabharati college of pharmacy Amravati SRPF Camp Rd, near Collector Office, Maltekdi, Amravati, 444602.*
Email : prachivgupta9881@gmail.com

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inflammatory, antidiabetic, antileishmanial, and antitumor activities. (1)

Apart from its ornamental value, Kalanchoe is also very well known as a medicinal plant in the folk medicine. In recent years, an increased interest in the phytochemistry of the genus Kalanchoe which reported to contain interesting biologically active constituents such as bufadienolides, flavonoids, triterpenes and sterols that constitute the major secondary metabolites and showing interesting spectrum of activities.(2)

Plants of the genus are widely used in traditional medicine in several countries, including India, China, South Africa and other African nations, and Brazil, as well as in alternative medicine systems. Indeed, in some of these countries, we can find reports of the use of Kalanchoe plants in Ayurveda, Chinese Traditional Medicine, and anthroposophic medicine. In particular, in Brazil, K. pinnata is part of a list of medicinal plants to be used in the national public health system (SUS-Sistema Único de Saúde). Among the ethnomedicinal uses, plants of the genus are reputed therapeutics in the treatment of inflammatory conditions, wounds, gastric ulcers, genito-urinary disorders, and other illnesses (3).

1. BOTANICAL DESCRIPTION :

1.1 Taxonomy:

- **Plant Name:** Kalanchoe tomentosa
- **Common Name:** pussy ears or panda plant
- **Synonyms:** Panda plant

➢ TAXONOMIC POSITION :

- **Kingdom:** Plantae
- **Subkingdom:** Tracheophytes
- **Super division:** Angiosperms
- **Class:** Eudicots
- **Order:** Saxifragales
- **Family:** Crassulaceae
- **Genus:** Kalanchoe
- **Species:** K. tomentosa baker
- **Botanical name :** Kalanchoe tomentosa (4,5,6)

Fig. kalanchoe tomentosa

1.2 Vernacular Names :

- **Commonly known as:** Panda plant, pussy ears, chocolate soldier, cat ears, donkey ears, cocoon plant.
- **Other languages:**
- Bahasa Indonesia: Kaktus panda
- Dutch: Pandaplant

1.3 Morphology :

□ **Habit**

- *Kalanchoe tomentosa* is a **perennial succulent shrub**, native to Madagascar.
- It grows **30–50 cm** tall in cultivation but can reach up to **1 m** in natural habitats.
- The plant exhibits **woody basal stems** and **tomentose branches**.
- Common names: *Panda Plant*, *Pussy Ears*. (7,8)

□ **Stem**

- **Erect or leaning**, cylindrical, densely covered with **white to silvery tomentum** (felt-like hairs).
- **Young stems** are soft and succulent, while **older ones** become woody.

- Serves as **water-storage tissue**, typical of xerophytic plants.(9)

□ **Leaves**

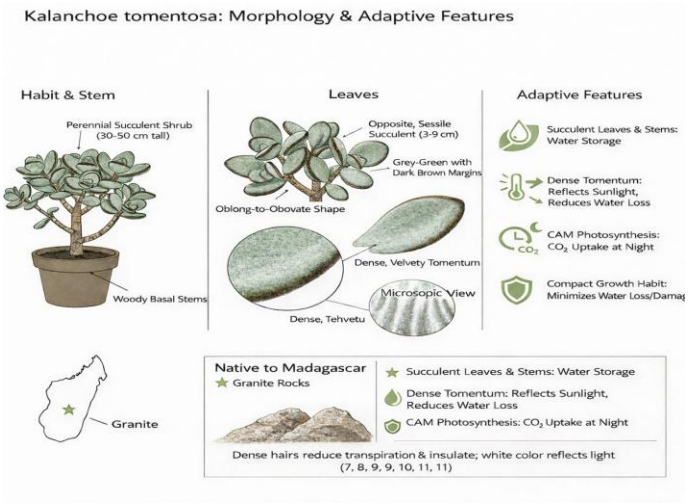
- **Arrangement:** Opposite or sub-opposite, densely crowded near stem tips.
- **Type:** Simple, sessile, fleshy, and succulent.
- **Shape:** Oblong to obovate, occasionally spatulate.
- **Size:** 3–9 cm long × 1–3 cm wide.
- **Color:** Grey-green with dark brown or reddish margins.
- **Surface:** Covered with **dense, velvety hairs (tomentum)**; lower surface convex, upper slightly concave.
- **Margin:** Entire or slightly crenate; teeth with **reddish-brown tips**.
- **Venation:** Reticulate, indistinct due to succulence. (8,9,10)

□ **Adaptive Features**

- **Succulent leaves and stems** store water for dry periods.
- **Dense tomentum** reflects sunlight and reduces evaporation.
- **CAM (Crassulacean Acid Metabolism)** photosynthetic pathway allows CO_2 uptake at night.
- **Compact growth habit** minimizes water loss and mechanical damage. (10)

1.4 Distribution :

Kalanchoe tomentosa is a succulent sub-shrub native to Madagascar. It is found on granite rocks, growing up to 45cm (1.5 feet) tall. The dense covering of hairs performs a vital function for the plant as a water conservation adaptation. In the dry environment in which it lives, the plant must conserve what little water it can absorb from the soil. The dense mat of hairs growing from the leaf retards the movement of air directly across the leaf surface, thereby reducing water vapor loss due to the transpiration process. At the same time, this unventilated space created by the numerous trichomes insulates the leaf from its harsh external environment, too. In addition, the white-silver appearance of the leaves reflects light, lessening the chances of the leaves overheating.

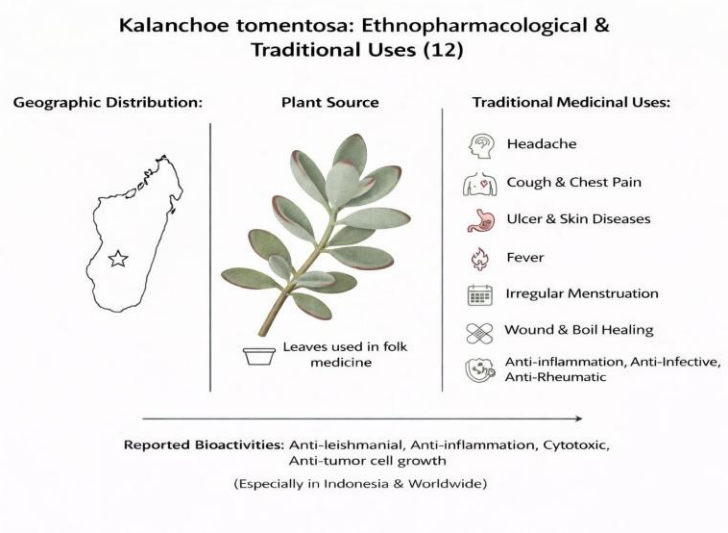


3. Ethnopharmacological and Traditional Uses :

Kalanchoe plants are used as traditional medicines to cure headache, cough, chest pain. ulcer, and other skin diseases. They overcome fever, fix the irregular menstruation, heal wound and boil, not only in Indonesia but also almost everywhere in the world. Some researches reported that Kalachoe plants contain bufadienolide, triterpenoid, and flavonoid, and biological activities like antileismanial, antiinflammatory, cytotoxic, and

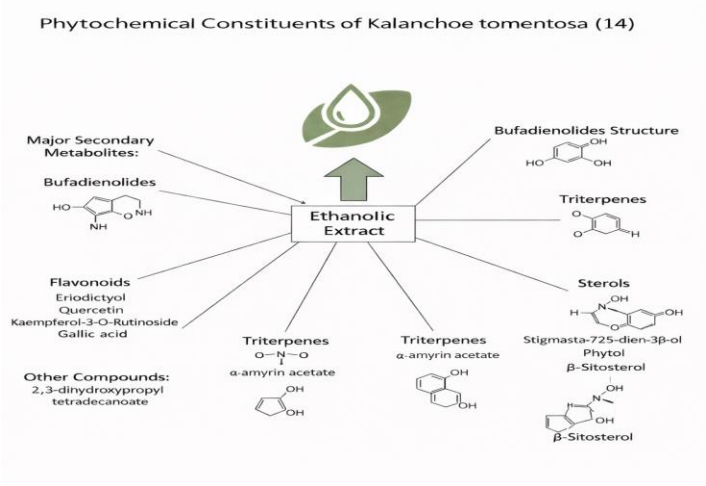
inhibiting tumor cell growth One of unknown Kalanchoe plants ethnopharmacologically is Kalanchoe tomentosa, especially its anticancer activity. (12)

The leaves of K. tomentosa are used in Indonesian folk medicine for the treatment of fever, infections, rheumatism, and skin diseases (13).



4. Phytochemical Constituents :

In recent years, an increased interest in the phytochemistry of the genus Kalanchoe has been reported to contain interesting biologically active constituents such as bufadienolides, flavonoids, triterpenes, and sterols that constitute the major secondary metabolites and show an interesting spectrum of activities. Phytochemical study of the ethanolic extract of Kalanchoe tomentosa (Crassulaceae) resulted in the isolation of 14 compounds identified as: α-amyrin acetate, friedelin, glutinol, 1-dotriacontanol, phytol, Stigmasta-7,25-dien-3β-ol, β-sitosterol, Isorhamnetin, 2,3-dihydroxypropyl tetradecanoate, Eriodictyol, Gallic acid, quercetin, kampferol-3-O-Rutinoside, and isovitexin (14).



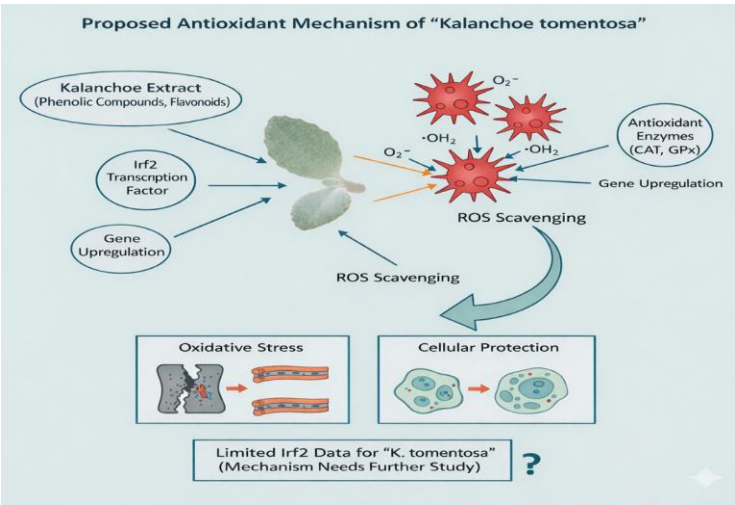
5. Pharmacological Activities :

5.1 Antioxidant activity

- The methanol extract of K. tomentosa was able to scavenge DPPH radicals: 50–150 µg/mL inhibited ~91 % of DPPH radicals; at 200-300 µg/mL ~92 % scavenging.
- The hexane and chloroform extracts showed much weaker DPPH scavenging (~36 % at 300 µg/mL for chloroform extract). (15)

➢ **Mechanism of action :**

Direct ROS/RNS scavenging: flavonoids and phenolic acids donate electrons/hydrogen to neutralize reactive oxygen species (ROS) and reactive nitrogen species (RNS) in cell-free assays (DPPH, ABTS, FRAP), explaining the high in vitro antioxidant capacity reported for K. tomentosa extracts. (15) Upregulation / preservation of endogenous antioxidant defenses: several Kalanchoe spp. extracts increase levels or activity of antioxidant enzymes (SOD, catalase, glutathione peroxidase) or prevent GSH depletion in cellular models - this is consistent with cytoprotective effects against oxidative stress. Mechanistically, flavonoids can modulate Nrf2 signaling in other plant extracts (hypothesized for Kalanchoe but dire Irf2 data for K. tomentosa remains limited). (16)

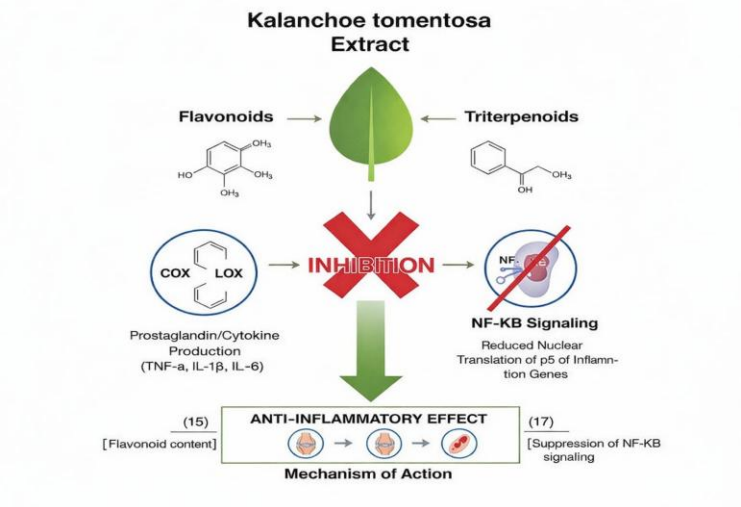


5.2 Anti-inflammatory activity

Traditional topical use for inflammation and wounds is supported by genus-level pharmacology and experimental reports showing inhibition of inflammatory markers by Kalanchoe extracts. Direct experimental data for K. tomentosa support anti-inflammatory potential via flavonoid content (15)

➢ **Mechanism of action :**

Inhibition of pro-inflammatory enzymes and mediators: flavonoids and triterpenoids in Kalanchoe extracts inhibit cyclooxygenase (COX) and lipoxygenase (LOX) activity in enzyme assays or lower prostaglandin/cytokine production (TNF-a, IL-1ß, IL-6) in stimulated macrophage models. Suppression of NF-KB signaling: several Kalanchoe species show suppression of NF-KB activation (reduced nuclear translocation/phosphorylation of p65) resulting in decreased transcription of inflammatory genes; by analogy, K. tomentosa flavonoids are likely to act similarly, though direct mechanistic NF-KB studies on K. tomentosa remain limited (17)



5.3 Antimicrobial / Antibacterial activity

- A dichloromethane extract (and the isolated β-sitosterol) from K. tomentosa leaves exhibited bacteriostatic activity against Staphylococcus aureus (MIC = 15.63 µg/mL for the extract, 7.81 µg/mL for β-sitosterol) and against Klebsiella pneumoniae (MIC = 7.81 and 31.25 µg/mL respectively).
- In the profiling study, however, the extracts showed relatively weak antibacterial performance with $MIC_{90} > 500$ µg/mL for many strains.
- An in-silico docking study proposed that flavonoid glycosides from the methanol extract may interfere with the NAM/NAG peptide formation in gram-positive bacterial cell walls (a hypothetical antibacterial mechanism) (15,18)

➢ **Mechanism of action :**

Membrane perturbation and permeability changes: lipophilic constituents (fatty acids, sterols) and certain phenolics can disrupt bacterial/fungal membranes, increasing permeability and causing leakage of cytoplasmic contents.Enzyme and cell-wall biosynthesis inhibition: in silico docking on K. tomentosa flavonoids suggested interference with NAM/NAG peptide interactions important for gram-positive peptidoglycan formation - a plausible mechanism for reduced viability of Gram-positive bacteria in some assays. Bioactive single-compounds: ß-sitosterol isolated from K. tomentosa has shown activity against Staphylococcus aureus and Klebsiella pneumoniae in reported studies, indicating that isolated phytosterols contribute to the observed antimicrobial profile. (15)

5.4 Enzyme-inhibition / Antidiabetic potential

- One study (in Indonesian context) isolated β-sitosterol from K. tomentosa dichloromethane extract, and found inhibition of α-amylase enzyme: the extract had about 65 % inhibition whereas β-sitosterol alone 6.7 % under the conditions used.
- This suggests potential for antidiabetic (post-prandial carbohydrate-digesting enzyme inhibition) activity, but this is preliminary and only in vitro. (12)
- The antidiabetic potential of Kalanchoe tomentosa has been primarily attributed to its rich phytochemical profile and enzymatic inhibition activity. Phytochemical investigations reveal the presence of flavonoids, phenolic compounds, triterpenoids, and sterols, which collectively contribute to its hypoglycemic properties

through multiple biochemical pathways (15,17)

➢ **Mechanism of action :**

1. Inhibition of Carbohydrate-Hydrolyzing Enzymes :
One of the primary mechanisms involves the inhibition of digestive enzymes α-amylase and α-glucosidase, responsible for the hydrolysis of complex carbohydrates into glucose. An in vitro study demonstrated that the ethyl acetate fraction of K. tomentosa leaves, containing a flavonol compound (3,7,4′-trihydroxyflavonol), exhibited significant α-amylase inhibitory activity ($IC_{50} \approx$ 346 µg/mL) (19). This enzyme inhibition delays glucose absorption in the intestine, thereby reducing postprandial hyperglycemia — a mechanism similar to that of synthetic antidiabetic drugs like acarbose (20).

2. Antioxidant-Mediated β-Cell Protection :
Oxidative stress plays a pivotal role in pancreatic β-cell dysfunction and insulin resistance in diabetes. K. tomentosa extracts exhibit potent antioxidant activities, as evidenced by DPPH and ABTS radical scavenging assays (15,17). These antioxidant compounds scavenge reactive oxygen species (ROS), protect β-cells from oxidative damage, and improve insulin secretion efficiency. By preserving β-cell viability, the plant indirectly enhances glucose homeostasis and insulin activity.

3. Improvement of Insulin Sensitivity :
Although direct in vivo studies on K. tomentosa are limited, related species such as Kalanchoe pinnata and Kalanchoe daigremontiana have been shown to enhance peripheral glucose uptake and improve insulin sensitivity via modulation of the PI3K/Akt signaling pathway and reduction of pro-inflammatory cytokines (e.g., TNF-α, IL-6) (16,21). Due to the structural and phytochemical similarities among Kalanchoe species, it is plausible that K. tomentosa exerts comparable effects on insulin signaling mechanisms.

5.5Cytotoxicity / Toxicity / Other activities

- The profiling study reported that extracts of K. tomentosa had *high toxic effect* against the nematode Caenorhabditis elegans (a model organism) though they did *not* decrease viability of Artemia salina (brine shrimp).
- The above-mentioned ethanolic extract study (2014) also looked at cytotoxic and antimicrobial activities, though details on cytotoxic targets are less specified. (2,15)

➢ **Mechanism of action :**

A central mechanistic theme in Kalanchoe anticancer literature is the role of bufadienolides (cardenolide-like steroids) and other phenolics:
Na+/K+-ATPase inhibition (primary molecular target for bufadienolides):
bufadienolides bind to and inhibit the Na+/K+-ATPase (the same target as cardiac glycosides like digoxin). This inhibition disrupts ion homeostasis, causes intracellular Na+ accumulation → reduced Na+/Ca2+ exchange → increased intracellular Ca^{2+}, which can trigger mitochondrial dysfunction, activation of caspases, and apoptosis in cancer cells. Several Kalanchoe-derived bufadienolides display cytotoxicity correlated with Na+/K+-ATPase inhibitory PMC +1 potency.
Induction of apoptosis via mitochondrial (intrinsic) pathway: treated cancer cells show loss of mitochondrial membrane potential, cytochrome-c release, caspase-9/3 activation and DNA fragmentation. Some flavonoids and triterpenes also contribute to ROS generation that potentiates apoptosis.(22)

6. Future prospects for Kalanchoe tomentos

6.1 Novel bioactive classes worth pursuing :

- **Bufadienolides / cardiac glycoside–type steroids** — Kalanchoe spp. are a known source of bufadienolides with potent cytotoxic activity; these scaffolds are attractive starting points for anticancer lead optimization but require careful cardiotoxicity profiling. (23)
- **Flavonoids and sterols (e.g., β-sitosterol)** — recent phytochemical profiling of *K. tomentosa* found flavonoids and sterols with antibacterial and enzyme-inhibitory signals, suggesting both antimicrobial and metabolic (e.g., antidiabetic) lead options. (15)

6.2 Key research gaps :

- **Limited translational/PK data.** Most papers report in-vitro bioactivity or in-silico docking; there are very few in-vivo pharmacokinetics (absorption, distribution, metabolism, excretion) or formal ADME/Tox studies for *K. tomentosa* extracts or isolated compounds. (Implication: uncertain human safety margins.) (15)
- **Insufficient standardized chemical characterization and batch-to-batch controls.** Many studies use crude extracts without validated quantitative markers (e.g., no reference standards or validated LC-MS assays), making reproducibility and regulatory progress difficult. (15)
- **Mechanism-of-action gaps.** For promising activities (antibacterial, cytotoxic, antioxidant), precise molecular targets and downstream pathways are often not defined beyond in-silico hypotheses. This limits rational medicinal chemistry. (15)
- **Safety profile lacking for chronic exposure.** Cardiotoxic potential of cardiac glycoside-type compounds and possible cumulative toxicity is underexplored in chronic and reproductive toxicity models.(23)

6.3 Short-term (1–3 year) development priorities

- **Standardized extract and reference library** Build authenticated plant material banks, define voucher specimens, and develop validated UPLC-MS/MS assays to quantify 3–5 marker compounds (e.g., major bufadienolide(s), one flavonoid, β-sitosterol). This enables reproducibility and regulatory conversations. (15)
- **Bioactivity-guided fractionation + mechanism studies** Use activity-guided fractionation to isolate lead compounds; run target-deconvolution (affinity pulldown, CRISPR screens, proteomics) to identify molecular targets rather than relying only on docking. (16)
- **Early ADME/Tox and safety battery** Run in vitro hERG, cardiomyocyte assays, hepatic metabolism, and short rodent PK/Tox for prioritized leads (especially any bufadienolide derivatives). (23)

6.4 Medium-term (3–6 year) translational pathways

- **Medicinal chemistry on bufadienolide scaffold** to reduce Na^+/K^+-pump (cardiac) liability while preserving anticancer potency — i.e., SAR to separate cytotoxic vs. cardiotonic effects. Prioritize analogs with lower hERG/cardiomyocyte activity for in vivo efficacy models.(23)
- **Formulation & targeted delivery** — develop nanoformulations or targeted delivery (liposomes, antibody-drug conjugate strategies, tumor-targeting nanoparticles) that concentrate cytotoxic Kalanchoe derivatives in tumors and limit systemic exposure. This reduces cardiotoxic risk and improves therapeutic index. (Relevant because many

Kalanchoe compounds are highly potent but systemically toxic.) (24)

- **Combination / adjuvant strategies** — evaluate extracts/compounds as adjuvants to existing antibiotics or chemotherapies (synergy screens), particularly where in-vitro data suggest antibacterial or chemosensitizing effects. (15)

6.5 High-impact long-term directions

- **Biotechnological production & synthetic biology.** If specific bufadienolides or flavonoids are confirmed as leads, consider heterologous expression (yeast/plant cell cultures) or pathway engineering to avoid wild-harvest variability and supply bottlenecks. Tissue culture/regeneration protocols for *K. tomentosa* would support this. (25)
- **Derivation of non-cardiotoxic analogues** through scaffold hopping or prodrug approaches that activate selectively in tumor microenvironment (enzyme-cleavable prodrugs).(23)

6.6 Safety, regulatory and clinical gaps to address before human trials

- **Systematic cardiotoxicity testing** (acute and chronic), reproductive and genotoxicity studies, and well-controlled GMP production of lead(s). Cardiac glycosides historically have narrow therapeutic windows — regulators will require rigorous safety packages.(23)
- **Clinical indication selection.** Prioritize indications with high unmet need and clear route to clinical proof-of-concept (e.g., drug-resistant bacterial infections if antimicrobial potency and selectivity are confirmed; or refractory solid tumors if in vivo efficacy and safety permit). (15)

6.7 Practical recommendations for researchers / funders

- Fund **integrated projects** combining phytochemistry, target identification, ADME/Tox, and formulation (so a hit can progress rapidly to an in-vivo proof-of-concept). (15)
- Create **open-access spectral/biological databases** for *Kalanchoe* extracts (LC-MS, NMR, bioassay fingerprints) to avoid duplicated effort and accelerate SAR.(15)
- Prioritize **collaborations** between natural-product chemists, cardiotoxicity experts, medicinal chemists, and translational pharmacologists.

CONCLUSION

Kalanchoe tomentosa (Crassulaceae) represents a highly valuable medicinal plant owing to its rich phytochemical diversity and wide spectrum of pharmacological activities. Numerous studies have demonstrated the presence of bioactive compounds such as flavonoids, triterpenoids, bufadienolides, phenolic acids, sterols, and glycosides, which collectively contribute to its therapeutic potential. These metabolites are largely responsible for its reported antioxidant, anti-inflammatory, antimicrobial, antidiabetic, wound-healing, and cytotoxic properties, thereby validating many of its traditional medicinal uses.
Despite substantial preclinical evidence, current research on K. tomentosa remains limited by a lack of standardized extraction protocols, quantitative marker compounds, and in-depth mechanistic studies. Most investigations focus on in vitro or in vivo models without comprehensive pharmacokinetic, toxicological, or clinical assessments, which restricts its translation into evidence-based therapeutics. Additionally, the

potential cardiotoxicity associated with bufadienolide derivatives necessitates rigorous safety evaluations and structure–activity optimization. Future studies should emphasize the development of standardized extracts, advanced chromatographic and spectroscopic profiling, and bioactivity-guided isolation of lead compounds. Integration of molecular docking, omics-based target identification, and in vivo pharmacological validation can help elucidate the precise mechanisms underlying its therapeutic actions. Moreover, exploring novel delivery systems such as nanoformulations or biotechnological production of key metabolites could enhance bioavailability and therapeutic efficacy while ensuring sustainability. In conclusion, K. tomentosa is a promising reservoir of pharmacologically active molecules with potential applications in managing oxidative stress, inflammation, metabolic disorders, microbial infections, and cancer. Comprehensive, multidisciplinary research integrating phytochemistry, pharmacology, and formulation science is essential to transform this traditional medicinal plant into a modern, clinically relevant natural therapeutic.

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