The anti-cancer activity of *Kalanchoe tubiflora*

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**Abstract**

**Introduction**

Uncontrolled cell proliferation is a common feature of human cancer. Most of the drugs used currently in therapeutics strategies are classified as anti-proliferative drugs via apoptosis pathway. Mitotic catastrophe is a distinct non-apoptotic mechanism often triggered in cancer cells and tissues in response to anti-cancer drugs. As of date, little research exists to show Herbal extracts or plant-derived medicines are an important source of effective anti-cancer agents, particularly for treating mitotic catastrophe. This article explores how mitotic catastrophe is triggered by *Kalanchoe tuberculosis* and opens avenues for further research by presenting comparable results obtained so far.

**Conclusion**

For the past five years, we have been investigating the anti-cancer effects of *Kalanchoe tubiflora*, particularly to understand its action mechanism, and have analysed its efficacy through various in vitro and in vivo tests. Our preliminary studies show that *Kalanchoe tubiflora* is a potential anti-cancer agent and merits further investigation. The extract of *Kalanchoe tubiflora* inhibits cell proliferation and reduces cell viability through two mechanisms. First, it disrupts centrosome integrity and induces multipolarity; second, it perturbs chromosome alignment at metaphase. Both mechanisms specifically target mitotic cells, which leads to cell death.

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**Introduction**

Research on medicinal plants has shown that they are an important source of effective anti-cancer agents. More than half of the drugs used in clinical trials for anti-cancer activity are derived from natural sources. *Kalanchoe* is a genus of the Family Crassulaceae. Various species of *Kalanchoe* are used medicinally in Southeast Asia, specifically Indo-China and Philippines. Plants of this genus are mentioned in folklore and are used as traditional medicines for treating fever, abscesses, bruises, contused wounds, coughs, skin diseases, infections, hypertension, rheumatism and inflammation and, in particular, tribes in the state of Kerala, India, use these plants for treating cancer symptoms. A variety of bufadienolide compounds have been isolated from various *Kalanchoe* species, which showed strong anti-tumour-promoting activity.

In one of the above cases, *Kalanchoe hybrida* was used. It is the hybrid of *Kalanchoe daigremontiana* and *Kalanchoe tubiflora* (KT) and is naturalized throughout the island of Taiwan. On the basis of the aforementioned studies, KT, one of the origin sources of the hybrid, was selected as a target given its biological activities. KT is used as a wound-healing agent in traditional South Brazilian medicine. Few cardenolide and bufadienolide glycoside compounds were isolated from KT in Kuo group. Four of the isolated compounds have the capacity to arrest HL-60 cells in G2/M phase. In our study, we used KT as an example to discuss agents that target mitotic cells.

**Discussion**

The authors have referenced some of their own studies in this review. The protocols of these studies have been approved by the relevant ethics committees related to the institution in which they were performed.

**Anti-cancer activity**

Schmidt et al. carried out a study to establish the biological properties of Brazilian plants used in wound healing. By studying the different bioassays identified, Schmidt et al. found that KT did not show much promise as a potential treatment agent. In fact, KT showed a toxic effect in the MTT assay. This is consistent with the findings of our study. Toxicity of KT was tested in different cell lines and different dosages. The cell viability for all cell lines was found to be 20% below the concentration level of 20μg/ml. Hence, there is sufficient evidence to suggest that KT extract effectively inhibits growth of different cancer cell lines.

The scratch assay in Schmidt’s study showed that the n-hexanic extract of KT had no activity in the scratch assay at a concentration of 10μg/ml. The ethanolic extract showed a moderate ‘wounding-healing’ effect. However, in our study we found that KT extract completely blocked ‘wound healing’ at a concentration of 50μg/ml. Note that the scratch assay does not distinguish between migration and proliferation. However, in terms of anti-cancer activity, KT is a promising agent for anti-proliferation and/or anti-migration.

**Anti-cancer mechanism**

Mitosis is a highly coordinated process in which two copies of one chromosome are moved away from each other to the opposite poles of cells. Sister-chromatid segregation depends on a complex molecular scaffold of the mitotic spindle. Disruption of the mitotic spindle structure precludes proper alignment of chromosomes and activates the spindle assembly checkpoint and mitotic arrest, which
Critical review

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activate mitotic checkpoints and cause mitotic arrest. The arrested mitotic cells are often followed by cell death in mitosis. Some of the mitotic defective cells could exit mitosis and end up in a tetraploid or aneuploid state. The fate of those mitotic checkpoint slippage cells could be apoptosis, senescence or necrosis. Various compounds isolated from KT have been summarized in this critical review (Table 1).

### Conclusion

Finding ways to develop traditional herbal medicine is a matter of great urgency. Plants have chemical defence mechanisms that synthesize a wide variety of compounds that can be used to perform important biological functions and to defend against attack from predators. Many of these phytotoxins have beneficial effects, but some can have adverse or lethal effects on humans. However, no single chemical can effectively treat human diseases without side-effects. Isolation, identification and bioactive tests of pure compounds are standard strategies utilized in studying natural products. In many cases, scientists are not sure what specific ingredient in a particular herb can treat diseases. Whole herbs contain many ingredients that likely work together to produce a beneficial effect. Herbalists tend to use extracts from different parts of plants, such as roots or leaves, but do not isolate particular phytochemicals. They often reject the notion of a single active ingredient, arguing that the different phytochemicals present in many herbs will interact to enhance the therapeutic effects of the herbs and dilute toxicity. However, the activities of compounds isolated from plants are not necessarily parallel to the phenotypes observed in the traditional use of these plants.

A major aspect of traditional Chinese medicine focuses on restoring the homeostasis of the body to maintain health rather than treating a particular disease or medical condition. If used correctly, herbs can cure a variety of conditions, and in some cases, may have fewer side-effects than some of the conventional medications. Here we would like to draw an open question. Shall we keep doing separation? In understanding the role of medicinal herbs in human physiology, one might end up with putting all the isolated components together in order to reveal how therapy works. Hence, we still have a long way to go in determining the most effective modalities of treatment that uses medicinal herbs. More scientific data and evidence-based research are needed to determine the effectiveness of medicinal herbs.

### References

Critical review