SURE Rapid Response

Is there an application of Herbal Medicines (esp. *D. Erecta*) in the management of HIV/AIDS and Cancer?

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This rapid response was prepared by the Uganda country node of the Regional East African Community Health (REACH) Policy Initiative.

Key messages

- There is no compelling evidence to support the use of the herbal medicines identified in the review for treatment of HIV infection and AIDS

  Overall there is a lack of evidence of the efficacy of most herbs in the treatment or prevention of cancer

- The leaves and berries of *D. erecta* are known to be toxic causing skin irritation (dermatitis), gastro enteric irritation, drowsiness, fever, nausea, vomiting, convulsions, and death in some cases

- Other species in the Verbanaceae family have been found useful in the treatment of fever and diabetes, as remedies for conjunctivitis, venereal diseases and as laxatives. They in addition exhibit antimalarial, spasmolitic, sedative, hypotensive and anti-inflammatory activities

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SURE Supporting the Use of Research Evidence

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EVIPNet EVIDENCE-INFORMED POLICY NETWORK

Who requested this rapid response?

This document was prepared in response to a specific question from a policy maker in Uganda.

! This rapid response includes:

- Key findings from research
- Considerations about the relevance of this research for health system decisions in Uganda

X Not included:

- Recommendations
- Detailed descriptions

What is SURE Rapid Response Service?

SURE Rapid Responses address the needs of policymakers and managers for research evidence that has been appraised and contextualised in a matter of hours or days, if it is going to be of value to them. The Responses address questions about arrangements for organising, financing and governing health systems, and strategies for implementing changes.

What is SURE?

SURE – Supporting the Use of Research Evidence (SURE) for policy in African health systems - is a collaborative project that builds on and supports the Evidence-Informed Policy Network (EVIPNet) in Africa and the Regional East African Community Health (REACH) Policy Initiative (see back page). SURE is funded by the European Commission's 7th Framework Programme.
www.evipnet.org/sure

Glossary

of terms used in this report:
www.evipnet.org/sure/rr/glossary

Background

People with chronic illnesses often seek and use complementary medicines including herbal preparations for a number of reasons; many times they may turn to them when they feel conventional medicine is 'failing' them or when they are convinced about the effectiveness of the complementary medicines (1). Several plant or plant parts have been suggested for use (or are already in use) in many different treatment modalities but how effective and safe they are has always been a point of concern for health care providers and decision makers.

Herbal medicines also referred to as phytotherapeutic agents, are among the most popular of complementary therapeutic modalities. According to the World Health Organization definition, herbal drugs contain as active ingredients plant parts or plant materials in the crude or processed state plus certain excipients, i.e., solvents, diluents or preservatives (2-4).

Although the adverse effects of phytotherapeutic agents are less frequent compared with synthetic drugs, well-controlled clinical trials have confirmed that such effects do exist (2), and therefore all herbal drug use needs to be monitored and regulated.

The National Drug Policy/Authority (NDP/A) Act chapter 206 of the Uganda Laws mandates the National Drug Authority to regulate manufacture, registration and sale of herbal medicines in Uganda; to this end, in July 2009, guidelines for the regulation of traditional/herbal medicines (local) were released to provide guidance on this in the country (5).

The application of herbal medicines to the treatment of chronic illnesses like HIV and cancer is still undergoing a lot of research but we present here findings from the current literature.

NB: *Duranta erecta* is pointed out in this paper; the policymaker asking this question was especially interested in *D. erecta* and its *Verbanaceae* family

How this Response was prepared

After clarifying the question being asked, we searched for systematic reviews, local or national evidence from Uganda, and other relevant research. The methods used by the SURE Rapid Response Service to find, select and assess research evidence are described here:

www.evipnet.org/sure/rr/methods

What the quality of evidence (GRADE) means

The quality of the evidence is a judgement about the extent to which we can be confident that the findings of the research are correct. These judgements are made using the GRADE framework, and are provided for each outcome. The judgements are based on the type of study design (randomised trials versus observational studies), the risk of bias, the consistency of the results across studies, and the precision of the overall findings across studies. For each outcome, the quality of the evidence is rated as high, moderate, low or very low using the definitions below.

⊕⊕⊕⊕
High: We are confident that the true effect lies close to what was found in the research.

⊕⊕⊕◯
Moderate: The true effect is likely to be close to what was found, but there is a possibility that it is substantially different.

⊕⊕◯◯
Low: The true effect may be substantially different from what was found.

⊕◯◯◯
Very low: We are very uncertain about the effect.

For more information about GRADE:

www.evipnet.org/sure

What we found

Use of herbal medicines to treat HIV/AIDS

The majority of people living with HIV/AIDS are using complementary medicine (6). With the chronicity and impact of HIV and its related opportunistic infections affecting the quality of life of individuals, patients with HIV/AIDS are likely to seek use of, or try out as many treatments as possible to better their condition. To this end they will tend to combine use of orthodox medicines with complementary ones and this may be especially so in areas of the world where Antiretroviral Therapy is not available or is limited due to economic constraints (6). Although there are still gaps in knowledge about complementary and alternative medicines, the number of randomized trials of these has increased tremendously over the last two decades, doubling every five years (7). While some clinical studies done have shown that some herbal medicines might have the potential to alleviate symptoms, and in addition reduce viral load, and increase CD4+ cells in PLWHA, others have also shown the potential harm these might have on the patients; there is an increasing number of reports about liver toxicity and other adverse events from some herbal products, as well as possible herb-drug interactions (1). A recent systematic review was done to assess the beneficial and harmful effects of herbal medicines on patients with HIV infection or AIDS compared with no intervention, placebo, or antiretroviral drug. The outcomes of interest considered were mortality and morbidity, adverse events, immunological and virological responses, quality of life (1). They concluded that there is no compelling evidence to support the use of the herbal medicines identified in the review for treatment of HIV infection and AIDS (see table below).

Herbal medicines for treating HIV infection and AIDS

Patients or population: Male or female patients of any age or ethnic origin who have HIV infection, HIV related disease, or AIDS
Settings: USA, France, China, Switzerland
Intervention: Herbal medicines
Comparison: Placebo

Outcomes	Impact		Studies (Number of subjects)	Quality of evidence
	Effect size	Absolute change		
1. Occurrence of AIDS-related events SPV30 vs placebo	0.12 (0.01, 1.08)	Those receiving SPV30 were eight times less likely to have AIDS related events than those receiving placebo	1 (145)	⊕⊕⊕◯ Moderate
2. CD4 cell count less than 20 millions per litre SPV30 vs placebo	0.74 (0.33, 1.69)	The CD4 cell count of those receiving SPV30 was 1.35 times likely to be less than 20 millions per litre than for those receiving placebo	1 (145)	⊕⊕⊕◯ Moderate

3. Overall health perception (no. improved) IGM-1 (Chinese herbs) vs placebo	 0.75 (0.20, 2.79)	The overall health perception improved in the intervention group by 1.33 times compared to the placebo group	1 (30)	⊕⊕⊕◯ Moderate
4. CD4 cell count (X 10 6/L) SPV30 (990mg/day) vs placebo SPV30 (1980mg/day) vs placebo Chinese medicinal herbs vs placebo	 *39.70 (-14.00, 95.40) *16.0 (-35.12, 67.12) *-80.0 (-183.25, 23.25)	There was no significant difference in CD4 cell count in people treated by SPV30 or with Chinese medicinal herbs after 30 weeks compared with placebo	 1 (96) 1 (97) 1 (68)	⊕⊕◯◯ Low
5. Viral load (log unit or copies/ml) SPV30 (990mg/day) vs placebo SPV30 (1980mg/day) vs placebo Chinese medicinal herbs vs placebo Qiankunning vs placebo	 *0.11 (-0.22, 0.44) *-0.15 (-0.49, 0.19) *20117.0 (-29673.20, 69907.20) *-0.16 (-0.52, 0.20)	There was no significant difference between SPV30 or chinese medicinal herbs or qiankunning and placebo with viral load	 1 (77) 1 (79) 1 (68) 1 (36)	⊕⊕◯◯ Low
6. Overall life satisfaction IGM-1 (Chinese herbs) vs placebo	 *0.66 [0.05, 1.27]	There was a significant increase in overall life satisfaction in the intervention group	 1 (30)	⊕⊕⊕◯ Moderate

*Effect size given in terms of mean difference

Use of herbal medicines to treat cancers

Many anti-cancer drugs are from plant –derived compounds including the commonly used vinblastine, vincristine, the camptothecin derivatives, topotecan and irinotecan, etoposide, among others. These are isolated from plants like *Catharanthus roseus* G. Don. (Apocynaceae), *Camptotheca acuminata* Decne (Nyssaceae), *Podophyllum peltatum* Linnaeus (Podophyllaceae) and *Taxus brevifolia* Nutt. (Taxaceae) (8). There is more research being carried out in this field and its goal is to identify major active single herb(s) in a composite formula for some diseases and further explore active compound(s) in the single herb(s).

A review to assess the safety and efficacy of herbal medicines commonly used by patients in an attempt to: prevent cancer; treat cancer; treat adverse effects associated with conventional cancer treatments was carried out and it concluded that although there is clear evidence that many patients diagnosed with cancer, or those worried about being diagnosed with the disease, use many forms of complementary medicines including herbal remedies, overall

there is a lack of evidence of the efficacy of most herbs in the treatment or prevention of cancer (9). The evidence suggests that some herbs may have a role in preventing cancer or as adjunct therapies for its treatment and so there is more work in progress on this, for example another recent review analyzed anticancer candidates in patents of dietary supplements and botanical drug products from herbal medicines and summarized current progress of these (8).

The case of *Duranta erecta*

Duranta erecta also known as *Golden Dewdrop, Pigeon berry, Skyflower* or *Aussie Gold* is of the *Verbanaceae* family. It is usually cultivated as an ornamental plant especially in tropical and semi- tropical areas. Although songbirds eat the fruit without any adverse effects, the leaves and berries of the plant are known to be toxic, and are confirmed to have killed children, dogs and cats (10). Saponins in the fruits and foliage cause gastroenteric irritation, drowsiness, fever, nausea, vomiting, and convulsions. One may also get a skin irritation (dermatitis) following any handling of the plant (11). On the other hand, ethyl acetate and aqueous extracts of this plant's leaves show significant anti-malarial activity in mice and when given in small quantities, its fruits have been used to treat intestinal worms (11).

Other species in the Verbanaceae family have been found useful in the treatment of fever and diabetes and as food (vegetable) and in relieving constipation in animals. The genus *Lippia* belongs to this family; *Lippia* species have a long history of traditional medicinal application especially in West Africa, some of which have been validated scientifically. They are mostly used in the treatment of respiratory and gastro intestinal disorders. In addition, they exhibit antimalarial, spasmolitic, sedative, hypotensive and anti-inflammatory activities. Furthermore the leaves made into tea-like infusions are used as remedies for conjunctivitis, venereal diseases and as a laxative. Most of these effects have been attributed to the glycolside, essential oils and other phytochemical components of *Lippia (12, 13)*.

Conclusion

The current literature suggests that there is little evidence to support the use of phytotherapeutic agents including D. erecta in the management of HIV/AIDS and cancer.

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Conflicts of interest
None known.

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