

EXPERIMENTAL VALIDATION OF THE HEPATOPROTECTIVE AND ANTICANCER PROPERTIES OF *Vernonia amygdalina*: A REVIEW

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ABSTRACT

Cancer and hepatic disorders are two important health problems of community health enhanced by metabolic and genetic disposition of individuals. *Vernonia amygdalina* (VA) is a medicinal shrub useful for the treatment of various diseases including cancer and liver diseases. It is often utilised as edible vegetable. This review aims at logically examining experimental evidences supporting the use of *V. amygdalina* in folklore medicine. Several databases including MEDLINE and 'Google search engine' were used to retrieve recent information on *V. amygdalina* uses in ethnomedicine. Selection of literature and abstracts was done randomly by authors on the basis of their relevance to the immediate review. Search yielded 512 results; critical appraisal of results reduced the tally to 6 for anticancer properties and 5 for hepatoprotective studies respectively. Their therapeutic potencies had relevance with phytochemical content of *V. amygdalina*. The experimental results support the widely accepted hepatoprotective and anticancer properties of *V. amygdalina* in traditional medicine.

Keywords: *Vernonia amygdalina*, Hepatoprotection, Anticancer

INTRODUCTION

Non-communicable diseases such as cancer and hepatic disorders have recently received an increasing interest by scientist. Results of epidemiological studies suggest that the incidence of this disease is on the increase largely associated with dietary patterns even though they also appear to be environmentally determined. More so, it has been estimated that 35% of cancer deaths may be related to dietary factors (Paul *et al.*, 2005). The liver is the metabolic rheostat of animals. It confers the ability to cope with a wide range of substances ranging from metabolic intermediates to xenobiotics. Its diversity in metabolism makes it susceptible to damage as well as determining the fate of potential toxicants (Gonzalez, 2005). Therefore, genotoxic compounds may act on the liver culminating in liver damage often as cirrhosis, fibrosis and at its worst hepatocellular carcinoma. Due to the polyphasic nature of cancer and hepatic diseases and its multi-etiological aspects, nutritional status of subjects

may be a significant factor that confers resistance to environmental hazards.

Vernonia amygdalina is a shrub common to tropical Africa (Argheore *et al.*, 1998). The bitter leaves are used as vegetable. Results of phytochemical analysis showed that *V. amygdalina* has rich content of saponin, sesquiterpenes and flavanoids. Some scientists have opined that the flavanoids and its saponins are the active principles which confer antioxidant and anti-tumor activities on the plant (Igile *et al.*, 1994). Though at the moment there is paucity of data on the exact mechanism by which *V. amygdalina* elicits therapeutic effects, results of experiments conform to its folkloric use. The objectives of this review are to determine from available literature the effectiveness of *V. amygdalina* in the treatment of experimental cancer and liver damages.

MATERIALS AND METHODS

The study included works done exclusively on *V. amygdalina* using scientifically accepted agents to induce hepatotoxicity and established cancer

Table 1: Selected studies supporting the anticancer activities of *V. amygdalina*

Method	Model	Results	Reference
<i>In vitro</i> test for inhibition cell growth	Cancer cell lines	Hexane, butanol and ethyl acetate extracts of <i>V. amygdalina</i> inhibited DNA synthesis	Oyugi <i>et al.</i> , 2009
<i>In vitro</i> anti-proliferative study	BT-549 Breast cancer cells	<i>V. amygdalina</i> inhibited cell proliferation and DNA synthesis	Grasham <i>et al.</i> , 2008
<i>In vitro</i> viability test on cancer cells	MCF-7 Breast cancer cells	<i>V. amygdalina</i> has minimal DNA damaging effects and reduces cell viability	Yedjou <i>et al.</i> , 2008
<i>In vitro</i> assessment of cell membrane permeability and efflux	MCF-7 Breast cancer cells	<i>V. amygdalina</i> compromises cell membrane permeability/potential, efflux, cytosolic activities and cell death	Opata and Izevbigie, 2006
<i>In vitro</i> determination of molecular targets of inhibitors in <i>V. amygdalina</i>	MCF-7 Breast cancer cells	<i>V. amygdalina</i> exhibits cytostatic activities. ERK signalling pathways are intracellular targets of <i>V. amygdalina</i> .	Izevbigie <i>et al.</i> , 2004
Quantitative measurement of gene expression of phase 1 and 2 enzymes in response to <i>V. amygdalina</i>	MCF-7 Breast cancer cells	<i>V. amygdalina</i> induces CYP 3A4 and microsomal epoxide hydrolase gene expression	Howard <i>et al.</i> , 2003

cell lines. *In-vivo* and *in-vitro* studies on the plants extract were considered however, data on clinical studies were not included. Databases such as MEDLINE and 'Google search engine' were used to retrieval of data. Search words used included *Vernonia amygdalina*, tumor, cancer, liver, hepatotoxicity and hepatoprotection.

The data obtained were extracted and classified based on experimental models used, aim of study and results obtained. Randomly selected literatures by the two authors where systematically put together to eliminate conflicts in data selection.

RESULTS

A total of 512 abstracts were retrieved from the databases amongst which where two reviews and six full text research articles. Six were eventually selected for their relevance as an anticancer and five relating to hepatoprotection.

41 were miscellaneous literatures while 460 were not relevant to this review. The results of the selected studies are presented in Tables 1 and 2. Tabulation is based on the methods used in the experiments, models used and results obtained by referenced authors. The methods for the preparation of extracts of *V. amygdalina* conform with standard scientific measures therefore, results from their usage were considered reliable.

DISCUSSION

The results of this study indicates clearly the efficacy of *Vernonia amygdalina* in curtailing the emergence and spread of cancer as well as protecting the liver from injury arising from physical and chemical assaults. *V. amygdalina* is prescribed by herbalist non-specifically for any disease type because of its effectiveness in the treatment of a wide range of ailments. Phytochemical studies on the plant reveal the

Table 2: Selected studies supporting the hepatoprotective activities of *V. amygdalina*

Method	Model	Results	Reference
<i>In-vivo</i> effects of pre-treatment with <i>V. amygdalina</i> against CCl ₄	Rats	Methanolic extracts of <i>V. amygdalina</i> administered for 5 weeks before CCl ₄ challenge ameliorated the increase in liver injury marker enzymes	Adesanoye and Farombi, 2009
<i>In-vivo</i> hypolipidemic effects of <i>V. amygdalina</i> pre-administration with high fat diet	Rats	<i>V. amygdalina</i> reduced the controlled lipid content of liver and serum	Adaramoye <i>et al.</i> , 2008 a
<i>In-vivo</i> effects of <i>V. amygdalina</i> on irradiation induced liver damage	Rats	<i>V. amygdalina</i> increased antioxidant defence systems and protects the liver from radiation induced damages	Adaramoye <i>et al.</i> , 2008 b
<i>In-vivo</i> hepatoprotective effects of <i>V. amygdalina</i> against acetaminophen-induced hepatic damage	Mice	<i>V. amygdalina</i> suppresses hepatotoxicity by attenuating lipid peroxidation and oxidative stress	Iwalokun <i>et al.</i> , 2006
<i>In-vivo</i> test for the hepatoprotective effects of sesquiterpene lactone content of <i>V. amygdalina</i> on CCl ₄ induced liver damage	Rats	Sesquiterpene lactone of <i>V. amygdalina</i> has anti-hepatotoxic activities comparable with that of Kolaviron an extract of <i>G. kola</i>	Babalola <i>et al.</i> , 2001

presence of flavanoids, saponin (Igile *et al.*, 1994). The triterpenes play dominant roles in determining fate of cancer cells used in various studies. Anti-oxidation by plant extracts is an important mechanism for disease treatment. Right now there is an increasing awareness implicating oxidative stress in several pathologies. The antioxidant potential of the flavanoids of *V. amygdalina* possibly attenuates the oxidative stress posed by chemical agents responsible for hepatic damages. It is conceivable that *V. amygdalina* may actively participate in the clearance of harmful (to the liver) and carcinogenic xenobiotics by the induction of phase 2 enzymes (Howard *et al.*, 2003). Parallel to that may be the up-regulation of the oxidant threshold of cancer cells by *V. amygdalina* which results in the inhibition of their growth, activation of the ERK signalling pathways and eventual death. Disruption of

cellular and organellar membranes has been a chemotherapeutic target in the past decade. Membrane potential and the bioenergetic profile of cells are the life wire that guarantees their survival. Hence, permeabilisation of membranes and altered efflux systems conforms to the anti-cancer mechanism elicited by other accepted anti-cancer plants (Opata and Izevbigie, 2006). More so that complementary is encouraged, radiotherapy could be concurrently used with administration of *V. amygdalina* to alleviate the negative effects of radiation on cells (Adaramoye *et al.*, 2008 a, b). It is interesting to note that *V. amygdalina* is a common plant and even though continuous consumption of this plant is necessary to obtain medicinal results but it is nutritionally achievable.

Conclusion: We recommend an increased attention on the research of *V. amygdalina*.

Researches herein reviewed points at the possibility of identifying potential chemotherapy for cancer and hepatic disorders without toxic effects associated with the consumption of other medicinal plants.

REFERENCES

- ADARAMOYE, O., OGUNGBENRO, B., ANYAEGBU, O. and FAFUNSO, M. (2008). Protective effects of extracts of *Vernonia amygdalina*, *Hibiscus sabdariffa* and vitamin C against radiation-induced liver damage in rats. *Journal of Radiation Research*, 49(2): 123 – 131.
- ADARAMOYE, O. A., AKINTAYO, O., ACHEM, J. and FAFUNSO, M. A. (2008). Lipid-lowering effects of methanolic extract of *Vernonia amygdalina* leaves in rats fed on high cholesterol diet. *Vascular Health and Risk Management*, 4(1): 235 – 241.
- ADESANOYE O. A. and FAROMBI, E. O. (2009). Hepatoprotective effects of *Vernonia amygdalina* (Asteraceae) in rats treated with carbon tetrachloride. *Experimental Toxicology and Pathology*,
- ARGHEORE, E. M., MAKKAR, H. P. S. and BECKER, K. (1998). Feed value of some browse plants from central zone of Delta State of Nigeria. *Tropical Science*, 38: 97–104.
- BABALOLA, O. O., ANETOR, J. I. and ADENIYI, F. A. (2001). Amelioration of carbon tetrachloride-induced hepatotoxicity by terpenoid extract from leaves of *Vernonia amygdalina*. *African Journal of Medicine and Medical Sciences*, 30(1-2): 91 – 93.
- GONZALEZ, F. J. (2005). Role of cytochromes P450 in chemical toxicity and oxidative stress: studies with CYP2E1. *Mutation Research*, 569: 101 – 110.
- GRASHAM, L. J., ROSS, J. and IZEVBIGIE, E. B. (2008). *Vernonia amygdalina*: anticancer activity, authentication, and adulteration detection. *International Journal of Environmental Research and Public Health*, 5(5): 342 – 348.
- HOWARD, C. B., STEVENS, J., IZEVBIGIE, E. B., WALKER, A. and MCDANIEL, O. (2003). Time and dose-dependent modulation of phase 1 and phase 2 gene expression in response to treatment of MCF-7 cells with a natural anti-cancer agent. *Cellular and Molecular Biology*, 49(7): 1057 – 1065.
- IGILE, G. O., OLESZEK, W., JURZYSTA, M., BURDA, S., FAFUNSO, M. and FASANMADE, A. A. (1994). Flavonoids from *Vernonia amygdalina* and their antioxidant activities. *Journal of Agriculture and Food Chemistry*, 42: 2445 – 2448.
- IWALOKUN, B. A., EFEDEDE, B. U., ALABI-SOFUNDE, J. A., ODUALA, T., MAGBAGBEOLA, O. A. and AKINWANDE, A. I. (2006). Hepatoprotective and antioxidant activities of *Vernonia amygdalina* on acetaminophen-induced hepatic damage in mice. *Journal of Medicinal Food*, 9(4): 524 – 530.
- IZEVBIGIE, E. B., BRYANT, J. L. and WALKER, A. (2004). A novel natural inhibitor of extracellular signal-regulated kinases and human breast cancer cell growth. *Experimental Biology and Medicine*, 229(2): 163 – 169.
- OPATA, M. M. and IZEVBIGIE, E. B. (2006). Aqueous *Vernonia amygdalina* extracts alter MCF-7 cell membrane permeability and efflux. *International Journal of Environmental Research and Public Health*, 3(2): 174 – 179.
- OYUGI, D. A., LUO, X., LEE, K. S., HILL, B. and IZEVBIGIE, E. B. (2009). Activity markers of the anti-breast carcinoma cell growth fractions of *Vernonia amygdalina* extracts. *Experimental Biology and Medicine*, 234(4): 410 – 417.
- PAUL, B., HAYES, C., KIM, A., ATHAR, M. and GILMOUR, S. (2005). Elevated polyamines lead to selective induction of apoptosis and inhibition of tumorigenesis by (–)-epigallocatechin-3-gallate (EGCG) in ODC/Ras transgenic mice. *Carcinogenesis*, 26: 119 – 124.

YEDJOU, C., IZEVBIGIE, E. and TCHOUNWOU, P. (2008). Preclinical assessment of *Vernonia amygdalina* leaf extracts as DNA damaging anti-cancer agent in the

management of breast cancer. *International Journal of Environmental Research and Public Health*, 5(5): 337 – 341.