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 multietiological 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 hepatoxicity and established cancer

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

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

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

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.</i> <i>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	V. amygdalina 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 hepatotoxocity 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.</i> <i>amygdalina</i> on CCl₄ induced liver damage	Rats	Sesquiterpene lactone of <i>V. amygdalina</i> has antihepatotoxic activities comparable with that of Kolaviron an extract of <i>G. kola</i>	Babalola <i>et al</i> ., 2001

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

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 anticancer 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). Lipidlowering 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* (Astereaceae) 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. Α., ODUALA, Τ., MAGBAGBEOLA, 0. A. and AKINWANDE, Α. 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-3gallate (EGCG) in ODC/Ras transgenic mice. Carcinogenesis, 26: 119 – 124.

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