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Effects of plants and medicinal plant combinations as anti-infectives

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The ascendancy of the Human Immuno Deficiency virus (HIV) has spurred intensive investigation into plant derivatives, which may be effective, especially for use in underdeveloped nations with little access to expensive western medicines. This review describes mostly the current state of anti microbial substances of plant origin ranging from extracts commonly in use, largely by the community, to substances being prospected screened and tested by researchers and clinicians. This review focuses on plant and their extracts, which are anti microbial in nature or in other words the anti microbial substances of plant origin and their eventual therapeutic effects on human affairs. Only phytochemicals or anti microbial substances reported to have anti microbial or anti-infective properties are examined.

Key words: Phytomedicines, medicinal plants, human, diseases.

INTRODUCTION

The study of higher plant for the purpose of detecting anti microbial agents in their tissues is of comparatively recent origin and the early investigation in this area focused on those plants that have found application in the age-old practice or their blind usage as therapeutics for human and animal diseases (Benjamine et al., 1983; Okigbo and Nmeka, 2005). The use of complementary medicines increased the interest of pharmacologist and herbalists over the past decade.

Historically, medicinal plants have provided a source of inspiration for novel drug compounds, as plant derived medicines have made large contributions to human health and well being. On the other hand, there is an increment of herbal products all over the world, in USA, it reached 38% between 1990 and 1997 (Eisenberg et al., 1990).

According to Arora and Keur (1999), the success story of chemotherapy lies in the continuous search of new drugs to counter the challenges posed by resistance strains of microorganisms. The investigation of certain indigenous plants for their antimicrobial properties may

yield useful results. Many studies indicate that in some plants there are many substances such as peptides, alkaloids, essential oils, phenols, coumarines and flavonols which confer antimicrobial properties to them. These compounds have potentially significant therapeutic application against human pathogens, including bacteria, fungi or virus (Arora and Keur, 1999; Okigbo and Igwe, 2007). The search for natural products to cure diseases represents an area of great interest in which plants have been the most important sources because of the prevalence of microbial resistance to existing synthetic drugs. In addition, in order to halt the trend of increased emerging and microbial resistance infectious diseases, it will require a multi prolonged approach that includes the development of new drugs (Iwu et al., 1999, Okigbo and Ajalie, 2005). Thus, evaluating plants from the traditional African system of medicine provide us with the clues as to how they can be used in the treatment of diseases (Okigbo et al., 2005).

The world Health organization (WHO) has estimated that up to 80% of the world's population rely on plants for their primary Health care. In Nigeria, a 1985 WHO survey estimated that up to 75% of the population patronizes traditional medicine (Omoseyindemi, 2003). Many of the drugs used in modern medicine were initially used in

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Table 1. Some African medicinal plants with their medicinal values.

Plant	Disease cured	Action	Usage
<i>Xylopia aethiopica</i>	Intestinal spasms, cough, post partum tonic, for lactation, stomach remedy, bronchitis, biliousness, dysentery, headache, female hygiene	Soothing, antispasmodic, remove biliousness, emollient, sedative	Poultice of the plant
<i>Garcinia kola</i>	Bronchitis, throat infections, relieve colic, head or chest cold, cough, liver disorder	Antibiotic, antispasmodic, soothing, sedative, ease cough, expectorant, choleric	Eating the seed of the plant
<i>Vitex doniana</i>	Gastroenteritis, diarrhea, dysentery, infertility, eye diseases	antimicrobial, invigorating and anti-inflammatory	The stem bark decoction
<i>Crytoplepis sanguinolenta</i>	Fever, malaria, urinary and upper respiratory tract infection, rheumatism, venereal diseases	Antiplasmodial, antiviral, antispasmodic, expectorant, anti-inflammatory	Hot poultice of dried root
<i>Euphorbia hirta</i>	Bronchial and respiratory disorders, urinary disorder, skin diseases, ocular diseases and dysentery	Soothing antispasmodic, regenerates skin, emollient antiparasite, anti-inflammatory, antimicrobial, antiviral, antibiotic, diuretic	Aqueous decoctions of the plant, latex of the plant for cuts and warts
<i>Ocimum gratissimum</i>	Respiratory infections, diarrhea, headache, ophthalmic (ocular) diseases, skin diseases, pneumonia, cough, fever, conjunctivitis	Anti-inflammatory, soothing, expectorant, invigorating, antiseptic, sedative, emollient	Aqueous and ethanol extracts of the leaves
<i>Citrus aurantifolia</i>	Nervousness, anxiety, insomnia, gastroenteritis	Sedative, mildly narcotic anti-inflammatory	Infusion of leaves & flowers (Orange blossom) ethanol and aqueous leaf extracts
<i>Cajanus cajan</i>	Sickle-cell anemia, ulcer, typhoid, fever, malaria	Anti-anemic because of phenylalanine	The seed

Source: (Okigbo and Mmeka, 2006).

in crude form in traditional or folk healing practices or other purposes that suggest potentially useful biological activity (Iwu et al., 1999). However, it has become necessary to investigate the anti microbial effect of these plants and drugs derived from them. Investigation of medicinal potentials of plants therefore may lead to the development of plant-based drugs.

Antimicrobials from phytomedicines

A vast number of plant species have been screened for antimicrobial actions (Ogunlana and Ramstad, 1975; Leven et al., 1979; Nair and Burke, 1990; Okigbo and Mmeka, 2006). In recent times, interest in this area has increased tremendously due partly, to certain disadvantages that are associated with the use of many synthetic antimicrobial agents and to the rising incidences of multi-drug resistance against these agents (Odama et al., 1997). These shortcomings include their toxicity, the

ability of organisms to develop resistance to the drugs previously known to be effective, and loss of potency of the drug with time. On the other hand, the merits of herbal medicine over orthodox drugs include; minimal or no side effects on the organic functioning of the body, consistent potency, and the fact that they are well absorbed and distributed in the area of infection (Cheij, 1988; Nkere, 2003; Okigbo and Omodamiro, 2006).

The role of plants in herbal medicine as the major remedy in traditional medicinal system has been in medical practice for thousands of year. The use of plants have made great contribution to maintaining human health and thus, a majority of the world's population in developing countries still relies on herbal medicine to meet their needs (WHO, 1991) (Table 1). Nigeria is one of the countries rich in rare and useful herbs, thus providing a vast area of medicinal plant research for novel drug development (Sofowara, 1993; Okigbo and Mmeka, 2006). Many of these plants are designated weeds and are used as

potherbs. Their healing powers as claimed by local medicinal practitioners range from headache through skin diseases to gonorrhoea and syphilis (Akobundu, 1987; Burkill, 1997). Other ailments treated with these medicinal plants include asthma, cough, diarrhoea, malaria, diabetes, bleeding, childcare, healing of wounds and sores and tooth extraction. Some of these medicinal plants are used as styptic and as simple laxative as cure for dysentery. They can be given to pregnant women or nursing mothers in food for various medicinal reasons. They are also good sources of pesticide (Burkill, 1997; Gill, 1992; Okwute, 1992; Okigbo and Nmeke, 2005; Okigbo and Ogonnaya, 2006). Many of these plants have leaves that are consumed as leafy vegetables. These vegetables have nutritional potentials that can be harnessed for dietary purposes of man (Edeoga and Gomina, 2000; Okigbo and Mmeka, 2008). The plant parts used include the leaves, roots, barks and stems. Some of these plants are also used as animal feeds on by local farmers who do not have money to buy expensive compounded commercial feed (Edeoga and Erita, 2001). Though a lot of the screened plants that have antimicrobial properties have not been used in modern medicine, their usage in traditional medical practice is fairly very high (Iwu et al., 1999).

Active chemical constituents of medicinal action of plants

Medicinal Plants contain physiologically active principles, which over the years have been exploited in trado-medical practice for the treatment of various ailments (Adebanjo et al., 1983). Knowledge of these active constituents made possible by the development of organic chemistry and pharmacology may be useful to determine the principles for the therapeutic action and elucidate the mechanisms of action of the synthetic preparations of new medicines, enabling drugs to be modified and made more effective (Cowan, 1999). The medicinal value of these plants lies in some chemical substances that produce a definite physiological action on the human body. The most important of these substances are alkaloids, tannins, terpenoids, glycosides, phenolics, saponins, flavonoids, quinines, lectins and polypeptides, and many others (Cowan, 1999, Okigbo and Igwe, 2007).

The medicinal value of plants lies in some chemical substrates that produce a definitive physiological action on the human body. *Ankaferd* comprises a standardized mixture of the plants *Thymus vulgaris*, *Glycyrrhiza glabra*, *Vitis vinifera*, *Alpinia officinarum* and *Urtica dioica* (Akkoc et al., 2008). Furthermore, Akkoc et al. (2008) reported that the antimicrobial activity assay was performed by agar well diffusion to assess the antagonistic activity of *Ankaferd* against 26 indicator strains including human pathogens and food spoilage, Gram-negative and Gram-

positive bacteria. *Ankaferd* was found to be active against all bacteria tested while nisin, the only commercial bacteriocin for food preservation, was inactive against Gram-negative indicator strains (Akkoc et al., 2008). Besides a high inhibitory activity against Gram-positive and Gram-negative bacteria, including human pathogens and food spoilage bacteria, *Ankaferd* was found to be more stable than nisin in different heat and enzyme treatments. Antibacterial activity of *Ankaferd* can be extended to extreme environmental conditions such as potential use of the preparation for the therapy of infectious diseases and preservation of different type foods from food-born pathogens or food spoilage bacteria (Akkoc et al., 2008).

Present use of plants as antimicrobials

It is estimated that today, plant materials are present in, or have provided the model for 50% of Western drugs (Robbers et al., 1996). Many commercially proven drugs used in modern medicine were initially used in crude form in traditional or folk healing practices, or for other purposes that suggested potentially useful biological activity. The primary benefits of using plant derived medicines are that they are relatively safer than synthetic alternatives, offering profound therapeutic benefits and are more affordable (Iwu, 1999; Okigbo and Mmeka, 2006).

Therapeutic benefits of medicinal plants

Much of the exploration and utilization of natural products as antimicrobials arise from microbial sources, and the discovery of penicillin led to later discoveries of antibiotics (Trease and Evans, 1972). Though soil microorganisms produce most of the clinically used antibiotics, higher plants have also been a source of antibiotics (Trease and Evans, 1972). Examples of these are the bacteriostatic and fungicidal properties of lichens, antibiotic action of allicine in *Allium sativum* (Garlic), and the antimicrobial action of berberines in goldenseal (*Hydratis canadensis*) (Trease and Evans, 1972). Plant-based antimicrobials have enormous therapeutic potential. They are effective in the treatment of infectious diseases, while simultaneously mitigating many of the side effects that are often associated with synthetic antimicrobials (Iwu, 1999). Effectiveness of plants as antimicrobial agents is hinged on their mode of action in the body. Generally, they have tropism for specific organs or systems in the body with resultant multiple effects on the body (Okigbo and Mmeka, 2006). Their actions often beyond symptomatic treatment of the disease. For instance, *H. canadensis* not only has antimicrobial activity, but also increases blood supply to the spleen, thus promoting optimal activity of the spleen to release mediating compounds (Murray, 1995).

Table 2. Phytotherapeutic sales in world market

Year	Europe						America	Asia
	Germany	France	Italy	U.K	Spain	Netherlands	U.S.A	India
1995							\$3.2billion	\$400million
1996								
1997	\$3.5billion	\$1.8million	\$700million	\$400million	\$300million	\$100million		
1998								
1999							\$5 billion	

Source: (Gruenwald, 1997; Calixto, 2000; Okigbo and Mmekka, 2006)

Table 3. Some African phytomedicinals in world market

Plant species	Action	Constituents	Countries
<i>Ancistrocladus abbreviatus</i>	Anti-HIV	Michellamine B	Cameroon and Ghana
<i>Corynanthe pachyceras</i>	Male stimulant	Corynanthidine, Corynanthine, yohimbine.	Ghana
<i>Tamarindus indica</i>	Insecticides	Pectins	Egypt
<i>Rauvolfia vomitoria</i>	Tranquilizer and antihypertensive	Reserpine, yohimbine	Nigeria, Zaire, Rwanda, Mozambique,
<i>Cinchona succirubra</i>	Anti malarial	Quinine	West African countries
<i>Syzygium aromaticum</i>	Dental remedy	Eugenol, terpenoids	East Africa countries, Madagascar
<i>Agava sisalana</i>	Corticosteroids and oral contraceptives	Hecogenin	Tanzania
<i>Physostigma venenosum</i>	Ophthalmia	Physostigimine (eserine)	Calabar (Nigeria), Ghana, Cote D'ivoire
<i>Prunus Africana</i>	Prostate gland hypertrophy	Sterols, triterpenes, n-docosanol	Cameroon, Kenya, Madagascar
<i>Catharanthus roseus</i>	Anti-Leukemia and Hodgkin's disease	Triterpenoids, tannins and alkaloids.	Madagascar
<i>Zingiber officinale (Ginger)</i>	Spice, Carminative and Medicinal products	Gingerol	Nigeria
<i>Chrysanthemum cinerariifolium</i>	Insecticides	Pyrethrins	Ghana, Kenya, Rwanda, Tanzania, South Africa

Source: (Elujoba et al., 2005; Okigbo and Mmekka, 2006)

Economic benefits of medicinal plants

There has been a renewed interest in natural products globally. This interest is as a result of consumer's belief that natural products are superior over conventional medicines (Iwu et al., 1999). This therefore resulted in a dramatic increase in sales of plant-based products. Sales of products in this market have increased dramatically in the last decade. Sales of botanical products in the United States have reached \$ 3.2 billion of the \$ 10.4 dietary supplement industry in 1996 (Table 2). A market-based illustration of the demand for plant-based antimicrobials is

demonstrated by looking at the sales and availability of the herbal products in the world market (Tables 2, 3). In reviewing the top botanicals used as anti-infectives, *Hydrastis* accounted for 4.7% of herb sales in 1995 in the U.S and anti-infective agents accounted for up to 24% of the pharmaceutical market (1992 Census of Manufacturers, 1994; Gruenwald, 1997). Analysis of commercial value of *Hypericum* (St. John's wort) showed a similar trend. Though *Hypericum* is antiviral, it is primarily used for its anti-depressant activity. In 1995, it was not among the top selling herbs, however by 1997, it had become an overnight success, with sales increasing to over 20,000%

(Aarts, 1998).

The potential for developing antimicrobials into medicines appear rewarding, from both the perspective of drug development and the perspective of phytomedicines. The immediate source of financial benefit from plant-based antimicrobials from the herbal products market (Table 3) offers many opportunities for those cultivating new crops, as many of the plants that are wild must be cultivated domestically today to match increasing demands (Iwu et al. 1999). For instance, *Hydratis*, one of the top selling antimicrobials in the US herbal market, represents an example of a herb that has undergone domestication in order to supply the demand of the herbal products market and also to curb its threatened extinction (Iwu et al., 1999).

Agricultural benefits of medicinal plants

A number of higher plants in Nigeria are traditionally noted for their pesticidal properties and some of these have been biologically and phytochemically screened for their activity and chemical constitution (Okwute, 1992; Okigbo and Mmekaka, 2006). In some cases the activity has been associated with specific compounds or classes of compounds. For instance, the fruits of *Piper guineense* (Schum and Thonn) have been found to exhibit significant insecticidal activity against the garden *Zonocerus variegatus* and the activity has been associated with the presence of a piperine-type amide, guineesine (Okwute, 1992). There are several local plants species whose extracts or biocides have proved efficacious in protecting yam produce before and after harvest (Okigbo, 2004; Okigbo and Nmeka, 2005; Okigbo and Ogbonnaya, 2006). The most popular one among them is *Azadirachta indica* A. Juss (neem). Formulations of extract of *A. indica* include Water Dispersible Powder (WDP), Dust Preparation (DP), Emulsifiable Concentrate (EC), Neem Seed Water Extract (NSWE) and Neem Cake Water Extract (NCWE) (Okigbo, 2004). The seeds of *A. indica* at 0.1 ppm have been found to prevent damage of at least 25 species of economic pest, to agricultural crops and stored products with no mutagenic activity and are highly biodegradable (Kloos and McCullough, 1987). This therefore provides an environmentally responsible health solution to the control of pests (Iwu, 1999; Okigbo and Mmekaka, 2006). Similarly, the fruit of *Dennettia tripetala* G. Baker (Fam. Annonaceae) has been investigated for its essential oil, which has been shown to be an effective protectant for stored grains such as cowpea and maize without affecting their viability (Osisiogu and Agbakwuru, 1978). It is most likely that the biological activity of the essential oil is due to the presence of the pungent principles, β -phenylnitroethane. A Nigeria species *Comphora africana* (A. Rich) Engl, found in the arid areas of Sokoto, Kano and Kastina is commonly burnt in homes as fumigant insecticide

against mosquitoes and as termite repellent (Hutchinson and Dalziel, 1958).

The result of phytochemical and antimicrobial screenings strongly indicate that some of the plants so far screened have desirable activity that can be cheaply harnessed for use in combating agricultural pest and infections (Okwute, 1992; Okigbo and Mmekaka, 2006).

Conclusion

Plants have forever been a catalyst for our healing. In order to halt the trend of increased multidrug resistance and emerging infectious disease agents, it will require continuous chemotherapeutic substance for novel drug production. Plants therefore will continue to remain a very rich source of novel compounds or substances for development of new drugs against so many infectious drugs.

It is however, not enough for us to know those plants that are curative in nature without making deliberate, efforts to investigate certain antimicrobial substances embedded in those plants that make them useful to human.

The use of plant extract in disease and pest control in place of pesticides and synthetic fungicides is encouraged since plant materials (phytochemical) are biodegradable and reduce pollutions due to agro-chemicals. Cultivation and conservation of such important plant are recommended. Therefore, since medicinal plants are effective and easily available, unguided usage should be discouraged. Apart from investigating their antimicrobial properties, their toxicity should be carried out with the view to determining their safety for human consumption.

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and size of the medicinal plant market is a vital step towards planning for both the conservation and sustainable use of the habitats of these plants as well as for ensuring continued availability of the basic ingredients used to address the health needs of the majority of the world's population. Kuipers, Duke and Cunningham both address the impact of the international herb trade on local stocks of medicinal plants. As international trade in medicinal plants grows to a multi-billion dollar industry, local harvesting patterns shift from sustainable local harvesting to commercial gathering with