

Promising Efficacy of the *Cola acuminata* Plant: A Mini Review

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Received 27 April 2014; revised 31 May 2014; accepted 7 June 2014

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Abstract

Cola acuminata also known as the bissi nut extract was originally endemic to Africa but is now present in a number of tropical countries including Jamaica. Despite its rich history of ethnomedicinal use and promising bioactivity, there still exists limited research on this plant. Exploring and compiling the ethnomedicinal usage, identified bioactivities and isolates of *C. acuminata* will prove useful in steering future directional research with the hope of reaping the plant's full beneficial properties. The plant's traditional use encompass; cancer treatment, an antidote for poisoning, suppressing one's appetite, increasing alertness, treating migraine and motion sickness, obtaining a state of euphoria in addition to being used in certain traditional practices. Because of the plant's copious ethnomedicinal use, researchers were led to believe that the low incidence of prostate cancer evidenced amongst Asians could be as a result of phytochemicals present in the bissi nut. Research conducted in our lab confirmed the anti-cancer potential of the plant and recent research has identified a number of secondary metabolites present in *C. acuminata* which could be responsible for the observed bioactivities. The plant has also shown promise as an anti-microbial agent. This paper confirms the efficacy of the bissi nut plant both as an ethnomedicine as well as warranting further research that may prove useful both in the pharmaceutical and nutraceutical industries.

Keywords

Bissi, *Cola acuminata*, Prostate Cancer, Breast Cancer, Cytotoxic

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1. Introduction

With circa 30% of its terrestrial plants being endemic [1], Jamaica is known for its rich biodiversity and its abundant usage of medicinal plants as ethno medicines. Referring to the study of traditional medical practice, ethnomedicine is interested in the cultural understanding of health, diseases and illness [2]. The practice of ethnomedicine is a multifaceted system which not only constitutes the understanding of plants being used as a source of healing but also social and spiritual as well [3]. Medicinal plants continue to play a critical role in drug discovery and development because of the vast structural diversity of molecules found in the plant kingdom, some of which become new drugs or leads for the development of new drugs [4]. Among the drugs which have been developed from ethnomedicine are: vinblastine and vincristine from *Catharanthus roseus* (the periwinkle) used for treating acute lymphoma, acute leukaemias etc., reserpine from *Rauwolfia serpentina* (Indian snake root) used for treating hypertension, aspirin from *Salix purpurea* (willow) used for treating inflammation, pain and thrombosis and quinine from *Cinchona pubescens* (cinchona) used for treating malaria [5].

The bissy nut, *Cola* sp., an evergreen originally endemic to West Africa was introduced to many tropical countries, Jamaica being one of them. It belongs to the *Sterculiaceae* family having more than 125 species [6] and is locally known as bissy, cola or kola nuts [7]. The cola nut fruit is shaped like a capsule (**Figure 1**) and is comprised of fleshy, irregularly shaped seeds which are pink, red or white when fresh, and become brown and hard once they are dried. The seeds are called nuts because of their bitter and astringent taste [8]. The plant's rich history of traditional use paved the way for cytotoxic and anti-microbial screens [9] in addition to identifying its key phytochemicals. These findings are highlighted in this review since research is so limited despite the promising efficacy of the bissy nut plant. Such findings should pave the way for future directional research on this plant and so provide a platform where optimized solutions for cancer and bacterial infections among others cancer be identified.

2. Use in Ethnomedicine

Chewing of the fresh *Cola acuminata* nut is a well-known practise of the Western and sub-Saharan native populations of Africa particularly in Northern Nigeria, Ivory Coast, Sierralione Liberia and Sudan [10]-[12], whereas the dried nuts are used as beverages and as pharmaceutical agents in Europe and North America [13]. Bissy has a bitter taste and high caffeine content [14]. It is used traditionally as a caffeine stimulant and it is chewed in many West African cultures individually or in a group setting and is often used ceremonially, be it at weddings, child naming, funeral, the presentation of tribal chiefs or guests [15]. Chewing kolanut can ease hunger cramps, stimulates digestion and is also used for euphoric qualities. Its effects are comparable to other xanthine containing herbs like cocoa and tea [16]; nonetheless, the effects are distinctively different as it produces a stronger state of euphoria and well-being [14]. It is thought to enhance alertness and physical energy, elevate mood, increase tactile sensitivity, and suppress appetite. It may also increase body temperature, blood pressure, and res-



Figure 1. Leaves of the bissy nut plant and the capsule shaped fruit.

piratory rate [17]. It has been used as a common additive to American and European soft drinks [17]. The plant produces fruit pods containing seeds that are used to treat poisoning, digestive disorders [18] and asthma [19]. Small doses are used to treat migraine, motion and morning sickness. In addition, it has been used to relieve inflammation disorders such as rheumatism and gout and has been administered to treat pneumonia and typhoid fever when great nervous irritability was present. Kola nut is also used to treat diarrhoea and has been used as a diuretic [20].

3. Pharmacological Effects of *C. acuminata*

3.1. Anti-Cancer Potential of *C. acuminata* Extract

Being the leading cause of death in Jamaica and the third leading cause of death worldwide, cancer is a disease of major concern and the search for compounds that can combat these deadly diseases is ongoing. Presently, 60% of chemotherapeutic drugs are from natural origin [21], however more often than not they are associated with insufferable side effects which make the hunt for other molecular entities or plant extracts an ongoing one. Because of its abundant enthomedicinal practices, the bissy but plant seemed ideal to be screened for anti-cancer potential even though the plant has no traditional use in that arena. Research from our lab showed that of the five solvents used (hexane, dichloromethane, acetone, methanol and water), the hexane bissy nut extract was most effective as it (160 µg/ml) killed 100% of breast (BC) and prostate (DU-145 and PC) cancer cell lines [22]. Further, research has shown that extracts from the bissy nut were cytotoxic against MCF-7 cell line [23] while Edrini and others [16] showed that reduction in cell viability of the cell line was through apoptosis (at 60 µg/ml) in which case less cells were present in the S and G2 phase of the cell cycle when compared to the positive control. Bissy nut was also shown to reduce the viability of LNCaP and DU145 with growth inhibition (GI50) of 15 ppm and 3.6 ppm respectively [24]. A significant increase in mRNA of anti-apoptotic genes; Bcl2 and Bax were observed in addition to an increase in protein and mRNA levels of androgen regulated genes. These results show that the bissy nut plant may provide a key for modulating breast and prostate cancers in an AR-dependent manner. Further research should be explored against other cell lines, in addition to mechanistic and *in vivo* studies. Additionally, the plant's chemopreventive properties from other angles can also be explored, such as testing its ability to inhibit the activities of CYP1 family of enzymes implicated in cancer initiation. The Rho proteins family of proteins is also known as the cellular switches and their modulation can be explored in cancer prevention and treatment. Such studies would determine confirm the anti-cancer potential of this extract and pave the way for nutraceutical and pharmaceutical treatment options.

3.2. Anti-Microbial Properties of *C. acuminata*

Microbial infections are of major importance to the medical arena since they are responsible for 90% of infections found in health care services. The occurrence of MDR bacterial strains seems to be the major cause of treatment failure [25]. Not only do they warrant concern in the medical arena but to food preservation as well. Presently there is growing global demand for consumers to reduce chemical preservation that can be unfavorable to human health [26] [27]. Subsequently the search for plant metabolites such as polyphenols, glycosides and alkaloids amongst others are currently undergoing detailed investigations in response to consumer requirements for fresher and more natural additive-free products [8] [28] [29]. Research shows that methanolic and aqueous extracts of *Cola acuminata* seeds displayed antimicrobial activity against; *Bacillus subtilis*, *Staphylococcus aureus*, *Escherichia coli*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa* and *Candida albicans* ranging from 8 - 24 mm and results compared well with Gentamicin and Nystatin [8]. Bissy nuts are also employed in the treatment of malaria, fever, ringworm, scabies, gonorrhoea and dysentery [30]. These results concur with the use of the plant in traditional medicine and implicate its promise as an anti-microbial agent. Further research can be conducted to identify key phytochemicals be them individual or a combination responsible for the observed bioactivities. Research can be extended to *in vivo* and clinical trials to confirm the anti-microbial properties and once again pave the way for nutraceuticals and or pharmaceuticals that can be used to treat certain infections especially those caused by current strains now resistant to existing anti-microbial treatments.

3.3. Other Biological Activity Properties of *C. acuminata*

The effects of fresh kola nut extracts on female Swiss Webster mice on post natal development and their off

spring was investigated and it was found that mice whose mothers were exposed to the kola nut extract showed a decline in the rate of post natal body weight gain but they experienced eye opening and hair gain relatively faster than their respective controls [31] implying kola nuts affects the utero development and the effects seem permanent. Kola nut was also shown to exhibit a depressive effect on biphasic locomotor activity in male mice models at high concentrations (10 mg/kg) [32]. Results obtained from limited human trials infer that kola nut may have some weight loss properties, positive chronotropic and weak diuretic properties. Animal studies show analeptic and lipolytic (fat-burning) properties [17]. More recent research shows that it stains the cytoplasm of various rat tissues which shows that it can be a suitable alternative for histological staining and so be more environmentally friendly and cost effective than synthetic dyes [33].

4. Phytochemistry

Kola nuts are rich in xanthine alkaloids such as theobromine (up to 0.1%), caffeine (0.6% - 3.0%) and kolatin [34]. The plant contains 9.73% moisture, 2.72% ash, 3.02% fat, 19.14% protein, 7.3% crude fiber and 58.09% carbohydrate [35]. The plant is a source of other xanthine alkaloids, tannins, proanthocyanidins and anthocyanins such as “kola red”. Specimens of African kola yielded more caffeine (2.24 per cent) than Jamaican kola (1.93 per cent) [20]. The plant accumulates approximately 38% amino acids [34] and appreciable levels of appreciable levels of (+)-catechin, (-)-epicatechin, procyanidin B 1 [epicatechin-(4beta-->8)-catechin], and procyanidin B2 [epicatechin-(4beta-->8)-epicatechin] [35]. It also has higher levels of alkaloids, tannins and saponins than *Cola nitida* [35]. The phenolics and anthocyanins are likely to provide antioxidant activity [35] and the some of the active ingredients have been identified as non-steroidal compounds that are bioactive against prostate and breast cancer cells [23] [24] and so these compounds could be responsible for the observed bioactivity against breast and prostate cancer cell lines. The tannic acid in the kola nuts helps to precipitate a number of toxins in the gut preventing their absorption [22] hence its traditional use as an antidote. Given the potential anti-cancer and microbial properties, high throughput assays can be used to screen the known phytochemicals in hopes of identifying the individual ones or combinations responsible for the observed bioactivities. Further screens can be conducted on these to assess their potential chemopreventive properties.

5. Conclusion

Kola has been traditionally used for decades to treat cancer, enhance mental alertness, combat fatigue, as an antidote amongst many others. For this reason, researchers were led to explore the biological worth of this plant. So far, Kola promises to be an effective anti-cancer, anti-microbial and chemopreventive agent. Notwithstanding, despite its promising bioactivity, research on the plant is still quite limited and so further work is necessary to ensure the usefulness of Kola both in the pharmaceutical and nutraceutical industries. As a result, work is now being conducted in our labs to identify and quantify already identified and novel phytochemicals in addition to screen these against several other cancer and normal cell lines. Additionally, other bioactive screens are underway to confirm the plant's activity against other microbial organisms and we are in the process of exploiting the flavor and caffeine content of the plant extract to assist in the formulation of a sports energy drink.

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