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A Review Of Antiplasmodial Potentials Of Garcinia Kola

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Abstract: ***Garcinia kola popularly known as bitter kola is a member of the Guttiffarae, it is a tropical plant widely distributed around West African Countries including Nigeria. The seeds have been used in folk medicine and herbal formulations. G. kola constitutes phytochemicals such as; Anthraquinone, Kolaviron, Flavonoids, Saponins, Tanins and Saponins. The most prominent among them in the quest for newer antimalarial drugs is "Anthraquinone", which is the primary source of "Rufigallol"; a compound reported to be toxic against Plasmodium falciparum. The emergence of resistant strains of malaria causing plasmodium species is the greatest challenge against malaria control. However, Positive results from few experiments on the antiplasmodial potentials of G. kola have generated a lot of enthusiasm about its importance in the control of Malaria. This article is focused on reviewing current scientific write-ups relating to antimalarial potentials of G. kola extracts. A number of scientific experiments conducted confirmed the potency of the plant extract against Plasmodium spp in vitro and invivo. In spite of this, it is recommended that further research should be conducted at molecular level to enhance therapeutic modalities of its administration.***

Keywords: Garcina kola, Plasmodium, Antimalaria and Arthraquinone.

I. INTRODUCTION

Plasmodium is a parasite which infects the red blood cells and causes the disease known as Malaria. Of the species known to infect man, *Plasmodium falciparum* is the most deadly and predominant in Africa (Andare-Neto *et al.*,2004). Malaria is a tropical disease of public health importance endemic in Africa, Asia and parts of America. The World Health Organization reported that 335 Million people were at risk of catching Malaria (WHO, 2016). In 2012, an estimated 627,000 deaths was caused by Malaria globally, Africa being the most affected, recording for about 90% of all deaths worldwide (WHO, 2015).High rates of mortality and morbidity caused by Malaria seriously affects productivity and economic development. It accounts for about 15% of hospital admission and a leading cause of death in Nigeria. Most importantly it is a socio-economic problem which consumes about $5 million in various control attempts (WHO, 2002).

There is a major concern about the development of resistant strains of *Plasmodium falciparum* to most of the antimalarial drugs that are currently in use. This resistance has been attributed to factors such as production of substandard drugs and incomplete dose. The cost of qualitative antimalarial drugs in developing countries is discouraging, thus; patients seek other traditional alternatives from plant materials (Wilcox, 2004).

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Garcinia kola also known as Heckel belongs to the family Guttiferea and is a large forest tree which is valued in west and central Africa for its edible units (Hutchintson *et al.*, 1956). Extracts of the plant have been used traditionally for treatment of Lanryngitis, cough and other uses (YuHX, 2013). Asaolu, 2003 reported the presence of phytates, cyanate, arthraquinones and other phytochemicals in *G. kola*. It is of noteworthy, that, arthraquinones are the main source of Rufigallol; which is a compound known to be very toxic to *P. falciparum* (Winter *et al*., 1996). Furthermore, Damian *et al*., 2017, also reported that *G. kola* successfully reduced the percentage of parasitemia in albino mice infected with *Plasmodium berghei.* Positive results from these aforementioned and other similar experiments on the antiplasmodial potentials of *G. kola*, have generated a lot of enthusiasm about its importance in the control of Malaria. Therefore, article is focused on reviewing current scientific write-ups relating to antimalarial potentials of *G. kola* extracts.

Figure 1: Garcinia kola seed

A. ANTIMALARIAL COMPOUNDS FOUND IN *GARCINIA KOLA*

a. ANTHRAQUINONES

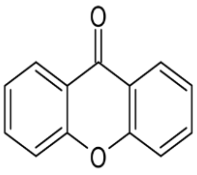
Anthraquinones also called dioxoanthracene is an aromatic organic compound with formula $C_{14}H_8O_2$. Several isomers are possible, each of which can be viewed as a quinine derivative. The term anthraquinones, however, almost invariable refers to one specific isomers 9, 10-anthraquinone (IUPAC: 9, 10-dioxoanthracene) where in the keto group are located on the central ring. It occurs naturally in *Garcinia kola, (Asoulu, 2003); (Tona et al.,2014); (Bello, 2018).* Derivative of anthraquinones include many important drugs (collectively called anthracenediones) they include antimalarial such as 1,2,3,4,5,6,7,- hexahydroxy-9, 10-anthraquinone, Rufigallol , 2,3,6,7-tetrahydroxy-9,10-anthraquinone, Octahydroxy-9, 10-anthraquinone . Findings of an inhibitory test of a series of hydroxyl and polyhyroxy-anthraquinones conducted against *P. falciparum, revealed that* "Rufigallol" demonstrated the most potent effect with a 50% inhibitory concentration (IC_{50}) value of ~ 10.5ng/ml (~ 35nM), (Winter *et al.,* 1995). Furthermore, Winter *et al*. (1996), uncovered a rare synergistic antimalarial interaction between Rufigallol and Exifone in choloroquine-susceptible and choloroquine resistance clones *P. falciparum.* In line with their findings, they went ahead to hypothesize that Ruffigalol acts in pro-oxidant fashion to produce oxygen radicals inside parasitized erythrocytes. These radicals would attack exifone, thereby initiating its transformation into a more potent compound, a xanthone.

b. FLAVONOIDS

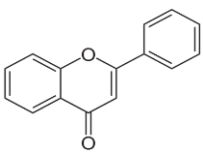
The term Flavonoid was first used by Hinreiner and Geisgman (1952), to embrace all those compounds whose structures are based on the aromatic nucleus of 2-phenylbenzopyron.The simplest of this class of compounds is flavones. Flavonoids are usually divided into classes depending on the oxidation level of the central pyron ring, the two most important classes being the flavonols or 3-hydroxylflavone (e.g quercetin) and the anthocyanidine (e.g cyaniding) . It occurs naturally in *G. kola*. Chemical analysis of the seed of *G. kola* unveiled the presence of biflavanones in Garcinia (GB), xanthones, triterpenes and benzophenones (5,17). The biflavanones are the most dominant in most *Garcinia* species (Waterman, *et al., 1983;* Benetode, 2015). Kolaviron, an extract from *G. kola* and a biflavonoid, has also been shown to exhibit antioxidant activity which is eventually assists in boosting the immune system to combat malaria parasites (Farombi, *et al.,* 2009). According to Benetode (2015), Kolaviron contains biflavonoids GB-1a, GB-1 and GB-2, that displayed potent inhibitory activity *in vitro* against *P. falciparum* and also antimalarial potency through oral administration in mice infected with *P. berghei*. In a similar study, kolaviron showed high antimalarial activity in *P. berghei* infected mice, especially 200mg/kg (Adaramoye *et al., 2014*).

c. XANTHONES

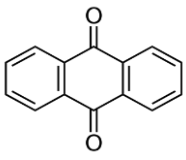
Xanthone is an organic compound with the molecular formular $C_{13}H_8O_2$. It can be prepared by the heating of phenyl salicate. In 1939, xanthone was introduced as an insecticide and currently finds uses as ovicide for codling moth eggs and as a larvicide (Steiner and Summerland, 1943). Xanthone naturally occurs in Garcinia kola (Adaramoye, 2012; Kenji et al., 1999). Five xanthones exracted from the bark of *Garcinia cowa*, namely 7-O-methylgarcinone E (1), cowanin (2), cowanol (3), cowaxanthone (4), and beta-mangostin (5), were reported to possess in vitro antimalarial activity against Plasmodium falciparum with IC50 values ranging from 1.50 to 3.00 micrograms/ml (Likhiwiyatayawid et al., 1998a,b).



Flavonoids



Anthraquinone



Xanthone

B. ANTIMALARIAL ACTIVITIES OF GARCINIA KOLA

An experiment conducted to test the protective activity of biflavonones obtained using bioassay-guided fractionation of a 70% ethanolic extracts of *G. kola* seeds, on P. falciparum (Benetode, 2015), revealed that the extracts displayed potent inhibitory activity *in vitro* against *P. falciparum* proliferation and also antimalarial potency via oral administration in mice

infected with *P. berghei* with no indication of acute toxicity. Out of the three biflavonone (GB-1a, GB-1 and GB-2) he isolated GB-1 was reported to exhibit the strongest *in vitro* antimalarial potency on *Plasmodium falciparum* with an IC_{50} of 0.16μM; whereas it exhibited a very low *in vitro* cytotoxicity on KB 3-1 cells with an IC_{50} of greater than 150μM. With respect to *in vivo* antimalarial assay in mice infected with *P. berghei*, GB-1 was found to exhibit biological potency with an approximate ED_{50} of 100 mg/kg following oral administration. GB-1 was also shown to increase the average life span of the infected mice significantly compared to that of control mice ($p < 0.01$) (Benetode, 2015).

In A similar study that investigated the antimalarial activity of ethanolic extract of *Garcinia kola* seed in mice infected with *Plasmodium berghei* (Damian *et al*., 2017) where Chloroquine was used as the reference drug. The results showed a significant reduction ($p \leq 0.05$) in percentage parasitaemia in the infected mice treated with Garcinia kola extract (Damian *et al*., 2017).

Also, KV2 significantly ($P<0.05$) increased the mean survival time of the infected mice by 175%. The biflavonoid prevented a drastic reduction in PCV from day 4 of treatment, indicating its efficacy in ameliorating anaemia. KV significantly ($P<0.05$) ameliorated the P. berghei-induced decrease in antioxidant status of the infected mice. The study also shows that kolaviron, at 200 mg/kg, has high antimalarial activities in P. berghei-infected mice, in addition to its known antioxidant (Adaramoye *et al*., 2014).

In another related study, extracts from bark, stem and seed of *Garcinia kola* inhibited the growth of *Plasmodium falciparum* recording over 60% inhibition *in-vitro*, at a concentration of 6 mg/ml (Tona *et al*., 1999). Administration of KV1 and KV2 significantly ($P<0.05$) suppressed P. berghei-infection in the mice by 85% and 90%, respectively, while CQ produced 87% suppression relative to untreated infected group after the fifth day of treatment. A similar study on the *in vitro* antiplasmodial activity of extracts and fractions of the stem bark of *Garcinia kola* Tona *et al*., (2004), also reported that EtOH extract and petroleum ether fraction has a significant antimalarial activity, which might be due to the presence of xanthones present in *Garcinia kola* (Likhiwiyatayawid et al., 1998a,b).

II. CONCLUSION

Taken together, we believe that *Garcinia kola* has remarkable antiplasmodial potentials that need to be explored. And if it is properly utilized, it will provide a cheaper and safer alternative for the treatment of Malaria. Therefore, additional research should be conducted at molecular level to enhance therapeutic modalities of its administration, and possible combination therapy potententials.

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