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Medicinal Uses of Cassia Sieberiana; A Review

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Abstract

Ethnomedicinal importance: *Cassia sieberiana*, mostly found in Africa has been used in traditional medicine as purgative, diuretic, analgesic, antibiotic, anti-inflammatory agent and many others for decades. This review focusses on discussions about its traditional therapeutic benefits, Ethnopharmacological studies, pharmacological, toxicological and phytochemical relevance. Materials and Methods: Electronic database such as PubMed, SciFinder, Science Direct, Google Scholar, Excerpta database and Springer were used in the search for filtered investigations on *Cassia sieberiana.* Results: The results from the various studies on *Cassia sieberiana* gave a detailed understanding of its constituents which serves as evidence for its therapeutic and safety importance as well as a source of novel compounds with therapeutic effects. Conclusion: This review on *Cassia sieberiana* is significant not only in providing a comprehensive data for continuous research but also will show untapped areas in the research on *Cassia sieberiana*.

Keywords: *Cassia sieberiana;* botanical description; pharmacology; toxicity; phytochemical constituents; Review

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1. Introduction

The use of plants to cure illnesses is probably as old as humankind [1]. According to the World Health Organization (WHO), more than 3.5 billion people in the developing world rely on medicinal plants as components of their healthcare needs [2]. One plant that is widely used for its therapeutic value is *Cassia sieberiana* DC (Fabaceae). *C. sieberiana* (also known as West African laburnum) is a tropical deciduous small tree. It is characterized by bright yellow flowers that form into groups (upright or hanging). Currently, there is no review that seeks to compile the pharmacological activities, phytochemical composition and reported toxicological studies on *C. sieberiana*. It has therefore become prudent to compile all available data on *C. sieberiana*. This study will go a long way to guide further studies on bioactivity guided isolation and purification of the different bioactive compounds responsible for the reported pharmacological and biological activities.

1.1. Taxonomy and Vernacular names

Cassia sieberiana DC. belongs to the kingdom Plantae, subkingdom Tracheobionta, phylum Angiospermophyta, superdivision Spermatophyta, division Magnoliophyta, class Magnoliopsida, subclass Rosidae, order Fabales, family Fabaceae, genus *Cassia* and species *sieberiana* [3]. *C. sieberiana* has several common and local names. Table one (1) contains the various local names by which the plant is referred to in different localities.

Table 1: Local Names

Country	Language	Local Name	Reference(s)
Ghana	Asante Twi Brong Dagbani Dangme Ewe Mole Kratchi	Progkese, Ekwo, Sanya Poto rodom Kotogyeben Kulphariyo Duotso Gagemagati Balepsado, Kikeliba, Nyaamde Konyan	[4]
Senegal	Arabic-Shuwa	Sindian	[4]
Guinea-Bissau	Bobo Dyula	Tenguele Canafistila	[5]
Burkina Faso	Lamare Fula- Fulfulde	Crioulo Sindian	[5]
Niger	Fula-Pulaar	Gama fadahi	[5]
Nigeria	Badyara	Sireih	[5]

1.2. Ecology

C. sieberiana is a shrub native to Africa. Its distribution spans across Africa including the southern part of the Sahel [6]. It grows best in well drained, humid soils with an annual rainfall of approximately 20 inches. These shrubs grow in groups of other plants; thus, they usually never grow alone [3]. It also grows in wooded grassland and savannah, secondary bush, on lateritic soils, roadsides, gravel and thickets, secondary (closed) forest, coastal scrub and sandstone plateau [7].

1.3. Botanical Description

Individuals range from 10-20m in height. The colour of the bark ranges from dark grey to black. The lenticels are horizontal and reddish in colour. The leaves are arranged in leaflets that contain 7-10 pair of opposite leaves. The upper side of the leaf is moderately shiny while the bottom has very fine nerves with stipules that are deciduous.[6] This plant has both flowers and fruit. The flowers are very bright yellow during the dry season, which is from February through to March. The flowers are also arranged either uprightly or in pendulous racemes ranging from 30–50 cm. September through to February is when the fruit reaches maturity. [6]

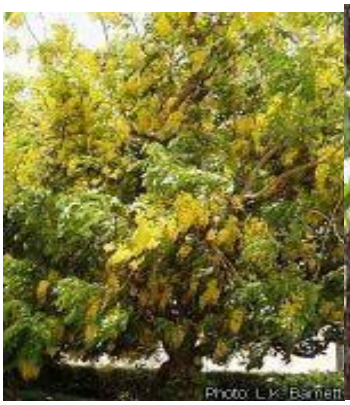

Figure 1: Flowering tree [5]

Figure 2: slash of stem bark[5]

Figure 3: Inflorescence [5]

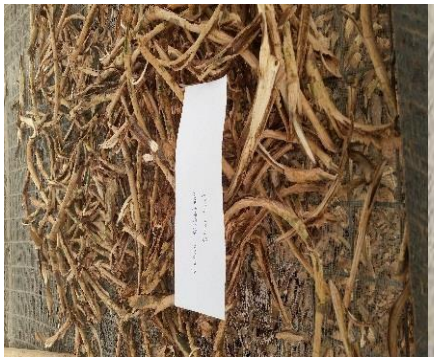

Figure 4: Stem bark (CPMR Arboretum)

Figure 5: Root [7]

Figure 6: Root bark (CPMR Arboretum)

1.4. Ethnopharmacological use of Cassia sieberiana

The leaves, roots and pods are widely used in traditional medicine [7]. Sleeping sickness is treated using the twigs. The liquid obtained after soaking the roots in water is used for a bath to remedy tiredness and also for body massage (Lim, 2012). A decoction of the bark, leaves or root is used for the treatment of dysentery, diarrhoea and vomiting the twigs are also used for the treatment of trypanosomiasis [7]. At the Center for Plant Medicine Research, the encapsulated root bark is used in the treatment of dysmenorrhea and pain associated with gastric ulcer. A summary of various conditions that can be treated with *C. sieberiana* and parts of the plant used is tabulated below.

Table 2: Ethnopharmacological use of *Cassia sieberiana* [7]

Plant Part	Mode of Preparation	Indication
Leaves	Infusion of the leaves sweetened with honey	Stomach ache, ulcer and diarrhoea
Leaves	Powdered leaves taking with food	Gonorrhea in women
Leaves	Boiled and squeezed fresh leaves applied as poultice	burns
Leafy twigs	steam bath of leafy twigs or decoction of leafy twigs can also be drunk	Fever and malaria attack
Pod	Infusion of pod and yellow pulp around the seed	laxative
Root bark	Infusion of the root bark	Sterility, dysmenorrhea, venereal diseases
Root	Decoction of root	aphrodisiac
Root	Boiled root in water	Hemorrhoids, bilharzia, leprosy, dropsy and blood dysentery
Root	Rubbing of crushed roots on the temples	headache
Root	A pinch of powdered dried decorticated roots taken at the end of each meal	Malaria prevention
Root	Debarked roots boiled with the bark of *Terminalia macroptera* Guill. and Perr.	Eczema
Different plant parts	A powder of different plant part mixed with butter	Skin diseases and toothache

2. Phytochemical Components

Various phytochemical constituents have been reported to be present in *C. sieberiana*. Its Seeds have been found to contain moderately high crude protein (23.72%), crude fibre (10.75%), potassium (252.33 mg/L) and magnesium (52.68 mg/L). Tannin, alkaloids, phenol, oxalate, cardiac glycosides and flavonoids are also present, while saponin is absent [8]. However, the pulp (fruit) revealed the presence of saponins together with tannins, alkaloids, steroids, flavonoids, phlobatannins, cardiac glycosides, cyanogenic glycosides and reducing sugars [9]. Saponins, anthraquinones, sterols, steroidal glycosides, tannins, triterpenes have also been reported in the root [10]. The root bark has high concentrations of some Phyto-constituents, with a total phenol concentration of 225.57±7.57 µg GAE/mg, total flavonoids of 64.70±5.25 µg QE/mg and total tannins of 170.60±5.85 µg TAE/mg [11]. The ethyl acetate fraction of the root bark also revealed the presence of saponins, flavonoids, anthraquinones and phenolics [12]. The aqueous extracts of the root bark and leaves revealed the presence of anthocyanosides, tannins, saponosides, reducing compounds, carbohydrates, flavonoids and triterpenic steroids. Alkaloid salts were however absent [13]. study on the root bark extract revealed the presence of saponins, flavonoids, anthraquinones and tannins. Furthermore, the root extracts reaction with $FeCl_3$ and their fluorescence under UV-light (Thin layer chromatography) indicated the presence of flavanol /flavonoid/flavone or related compounds with polyhydroxy and/or phenolic substances [14]. Phyto-constituents such as anthraquinones, flavonoid, saponins, steroid/terpenoids, tannins and cardiac glycoside have also been identified in *C. sieberiana* with moisture content of 6.2 ± 0.3 (%w/w), total ash, 5.8 ± 0.43 (%w/w), acid-insoluble ash, 1.0 ± 0.24 (%w/w), water-soluble ash, 3.5 ± 0.24 (%w/w), alcohol soluble extractive, 12.0 ± 0.47 (%w/w), water soluble extractive, 6.0 ± 0.47 (%w/w), Swelling index, 3.5 ± 0.00 (%w/w), foaming index of less than 100, tannins content, 39 (%w/w) and Bitterness value of 8400 unit/g [15]. Chemical analysis of aqueous leaf, stem, root and pod crude extracts of *C. sieberiana*

revealed the presence of alkaloids, tannins, flavonoids, saponins and phenols with percentage alkaloids (3.01±0.04, 1.44±0.00, 1.24±0.06 and 1.85±0.01), tannins (1.28±0.00, 1.12±0.01,

1.35±0.00 and 1.34±0.00), flavonoids (1.18±0.00, 1.74±0.00, 1.24±0.06 and 1.85±0.10), saponins (3.39±0.01, 2.20±0.03, 2.62±0.03 and 3.66±0.00) and phenols (0.29±0.01, 0.15±0.00, 0.19±0.00 and 0.25±0.00) respectively [16]

2.1. Isolated and Characterized Compounds

Fractionation and purification of various extracts of *C. sieberiana* has led to the isolation of a number of compounds. Using silica gel chromatography and Sephadex LH-20, eight compounds, islandicin, chrysophanol, physcion, emodin, quercetin, kaempferol, dihydrokaempferol and piceatannol, were isolated and characterized from the ethyl acetate fraction of root extract of *C. sieberiana* [17]. Also a main flavonoid component, epiafzelechin, has been isolated form the root bark extract using direct analysis in real time mass spectrometry, NMR spectroscopy, circular dichroism and optical rotation [18].

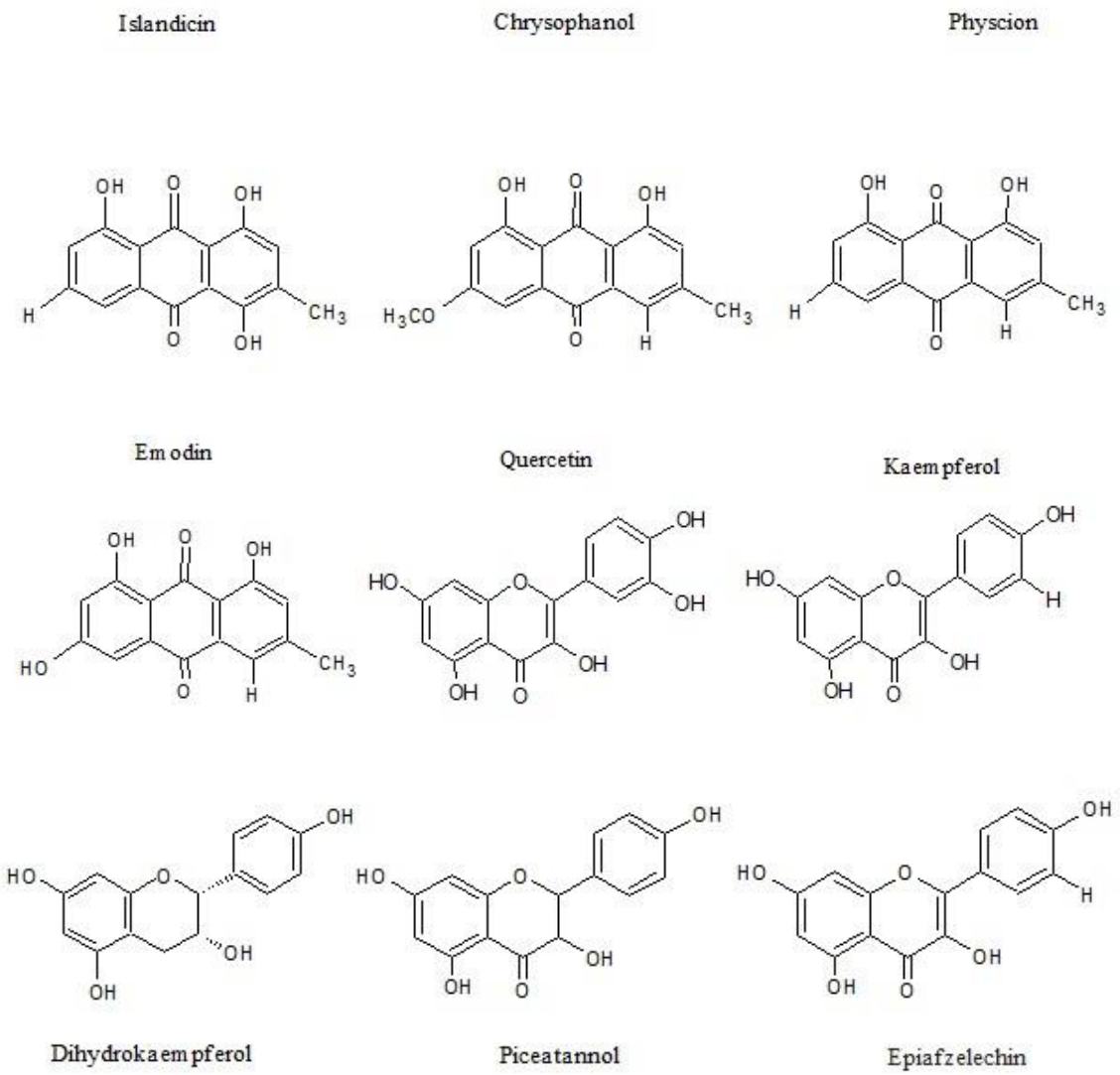

Figure 7: Chemical structures of isolated and characterized compounds from *Cassia sieberiana*

3. Pharmacological activity

3.1. Anti-inflammatory and anti-nociceptive effect

The serious undesirable side effects of the use of opioids, Non-steroidal anti-inflammatory drugs (NSAIDS) and non-opioids for the management of pain and inflammation has necessitated the search into natural products for a more affordable and less toxic alternative. Many plant extracts used in traditional medicine possess both antiinflammatory and analgesic properties. They are able to do this via the inhibition of COX 2 and inducible nitric oxide synthase by alkaloidic, tannic and flavonoidic compounds in them [19,20]. Guata Yoro Sy and his team in their work has demonstrated the presence of flavonoids and tannins in the aqueous root extract of *Cassia sieberiana*. This accounted for their observation of analgesic and anti-inflammatory properties of this extract; thus, at a concentration of 300 mg/kg per os, the aqueous root extract of *C. sieberiana* demonstrated almost identical analgesic activity as acetylsalicylic acid at a concentration of 100 mg/kg (20 ± 1.4 vs 26 ± 1.79 contortions) (ns, $p< 0.05$). Also, its anti-inflammatory activity was demonstrated by a significant reduction in carrageenan-induced oedema in rat paw oedema model ($p< 0.05$). This may be because of the suppression or prevention of inflammation process and pain by the flavonoids and tannins present [21]. Also, Donkor and his colleagues has investigated the anti-inflammatory and anti-nociceptive effect of the ethyl acetate fraction of the root bark of *Cassia sieberiana* DC using diverse rodent models. The carrageenan-induced rat paw edema test was used to investigate its anti-inflammatory property whiles its anti-nociceptive effect was also assessed using the hot plate test, formalin test, acetic acid writhing test and yeast-induced mechanical hyperalgesia test. The results from the carrageenan-induced rat paw edema test demonstrated a significant ($F_{3,19}= 4.59$, $p < 0.05$; ED_{50} =11.66±15.56 mg kg^{-1}) anti-inflammatory activity. Since this test model is a biphasic event [22], it is possible the ethyl acetate extract of the root bark of *C. sieberiana* exerted this anti-inflammatory activity via the inhibition of one or more mediators of inflammation. The oral administration of the extract dose-dependently and significantly inhibited both the second phase of inflammation ($F_{3,19}$=42.49, $p<0.0001$; ED_{50}=12.38±2.51 mg kg^{-1}) and the first phase of neurogenic response ($F_{3,19}= 30.87$, $p<0.0001$; ED_{50}=3.80±0.65 mg kg^{-1}) of the formalin-induced nociception in the experimental rats. It is only centrally acting medicines such as opioids that can inhibit equally both phases of nociceptive response [23]. This shows that, the ethyl acetate extract may be acting by both central and peripheral mechanisms to produce anti-nociception. Also, the inhibitory effect of the second phase corroborate its anti-inflammatory action. The demonstrated significant anti-nociceptive activity ($F_{3,19}= 57.95$, $p<0.0001$; ED_{50} = 6.99±1.78 mg kg^{-1}) against yeast-induced inflammatory pain also confirms its activity in the second phase (inflammatory pain) of the formalin test. The hot plate test which is mostly used to study central nociceptive activity demonstrated a significant ($F_{3,19}= 120.7$, $p<0.0001$; ED_{50} = 5.21±0.87 mg kg^{-1}) dose-dependent activity. This reinforces the involvement of central mechanisms in the anti-nociceptive effects of the ethyl acetate extract since the two behavior components measured, thus, paw licking and jumping (in terms of their increased reaction time) are considered supraspinally integrated responses [21]. The acetic writhing tests also involved the study of the possible involvement of adenosinergic, muscarinic cholinergic NocGMP, ATP-sensitive K^+ and opioid channels receptor systems in its anti-nociceptive effect. The intraperitoneal injection of acetic acid causes the release of inflammatory mediator which excites pain nerve. This sensitization of the nociceptive receptors to the prostaglandins causes abdominal constriction [24]. The extract showed a significant ($F_{3,19}$ = 89.88, $p<0.0001$; 9.34±2.01 mg kg^{-1}) dose-dependent reduction in the number of writhes (stretching of hind limbs and contraction

of abdominal muscle) of the tested rats. NSAIDS are known to reduce the number of writhes in this test via the inhibition of cyclooxygenase in peripheral tissues, thus blocking the synthesis and /or the release of inflammatory mediators [25]. It could be concluded that, the ethyl acetate extract of the root bark of *C. sieberiana* may be acting through a similar mechanism. Its anti-nociceptive effect may relatively be attributed to interactions with muscarinic cholinergic, adenosinergic and opioidergic systems [12]. This study also reported the presence of anthraquinones, saponins, phenolics and flavonoids in the ethyl acetate extract of the root bark of *C. sieberiana*. The presence of the saponins and flavonoids may be responsible for the anti-inflammatory and anti-nociceptive properties [26–28].

3.2. Management of Gastrointestinal disorders

Gastrointestinal disorders, being it peptic ulcer, diarrhoea, constipation and irritable bowel syndrome, chronic digestive syndrome, etc is among the most frequently encountered human disease [29]. *Cassia sieberiana* is among the reported plants used in traditional medicine in treating this ailment [7]. For this reason, some pharmacological studies have been done to confirm its therapeutic use;

3.2.1. Myorelaxant and antispasmodic activity

The study by Fall and his colleagues showed the pharmacological basis for the traditional use of *Cassia sieberiana* roots for the treatment of gastrointestinal disorder. The myorelaxant and antispasmodic activity of the crude ethanolic extract, the aqueous, ethyl acetate and butanol fractions were investigated on isolated wistar rat ileum. The crude ethanolic extract treatment at 75 µg/ml gave 50.51 ± 10.18% ($p<0.05$, $n=5$) as mean of inhibition percentage (MIP) of the basal tonus of rat ileum. However, the butanol and ethyl acetate fractions were more significantly active ($p<0.05$, $n=5$) on the ileal basal tonus than the crude ethanolic extract; thus, upon treatment with 37.5 µg/ml of these two fractions, the ileal basal tonus decreased with MIP of 60.61 ± 1.5% and 70.46 ± 5.18% respectively. However, the aqueous fraction was not active. Also, there was a significant decrease in spasm ($p<0.05$, $n=5$) when they were used for treatment in intestine precontracted with acetylcholine. This result shows that, the butanol and ethyl acetate fractions are more potent to induce antispasmodic and myorelaxant activity than the total ethanol extract [30].

3.2.2. Antioxidant and Gastric cytoprotective activity

Gastric ulcer disease is a complex disorder and among the various causes indicated in its pathophysiology is the implication of free radicals. As a result, the possible use of antioxidants is expected to prevent or heal gastric ulcers due to their ability to scavenge free radicals. To justify its phytotherapeutic application in gastric ulcer in West Africa, Nartey and his colleagues investigated the phytochemical, serum secretary phospholipase A_2, antioxidant, gastric cytoprotective prostaglandins and acute toxicity properties of the aqueous root bark extract of *Cassia sieberiana.* The results demonstrated that, this extract contains polyhydroxyl or phenolic substances (200 µg of freeze-dried extract yielded 75.32±0.52 equivalents polyphenols of gallic acid) which could have been responsible for its remarkable ferric reducing antioxidant activity (IC_{50} of 3.2±0.24 mg/ml) and can also scavenge

hydroxyl radicals (the crude extract at a concentration > 10mg/ml was able to achieve a maximum of 62% scavenging activity). Its significant 2,2-diphenyl-1-picrylhydrayl (DPPH) scavenging activity (at IC_{50} of 0.075±0.006 mg/ml, the scavenging activity of the crude extract was 63.2% of the IC_{50} value of L-ascorbic acid) could chelate ferrous ion at a dose dependent protective effect against free radical generation and lipid peroxidation (though its antioxidant activity was only 17% of that of L-ascorbic acid as illustrated by the peroxidation in the presence of 1mM linoleic acid, it has also shown a high chelating power via the decrease of free Fe^{2+} concentration). The prostaglandin studies also revealed that, the extract dose dependently increased gastric mucosal prostaglandin E2 (PGE2); thus, compared to the control, administering a dose of 250mg/kg increased PGE2 by 37.7%, 64.7% in those dosed with 500 mg/kg and finally by 82.4% in experimental animals dosed with 750 mg/kg. The prostacyclin (PGI2) and also decreased serum secretory phospholipase A2 (sPLA2) activity [14]. The flavonoids or polyphenols are able to prevent gastric ulcer via an increase in the amount of prostaglandin concentration and neutral glycoproteins as well as the obstruction of histamine secretion through the inhibition histidine decarboxylase. This results in either the secretion of prostaglandin-like compounds or the reduction in the stimulation of the H_2 receptors [31]. Another possible mechanism of action could also be due to a decrease in the secretion and activity of pepsin. Middleton and Kandaswami have also demonstrated the antiulcer activity of certain flavonoids through their direct mucosal protection activity similar to prostaglandins [32]. This shows that, the polyphenols or flavonoids may be responsible for the reported protection of the gastric mucosa as well as the anti-ulcer activity of the root bark extract of *C. sieberiana*, justifying its use in traditional medicine for the treatment of gastric ulcer.

3.2.3. Laxative activity

The presence of anthracene glycosides in *Cassia sieberiana* has been known to be responsible for its laxative property [33]. Ajayi and his team demonstrated the laxative activity of *Cassia sieberiana* using the official senna leaf (*Senna alexandrina*, family Caesalpiniaceae) as reference. The mean percentage of wet faeces produced by male albino rats who have been orally administered with 500 mg/kg of *Cassia* species in 12 hours, investigated alongside the reference drug under the same experimental condition at the same time gives an indication to its laxative effect [34]. This was carried out using previously established methods described by Lou [35] and Latven and his colleagues [36]. At 500 mg/kg, the stem-bark of *C. sieberiana* gave 36.0% wet faeces, 40.4% wet faeces by the root while the reference also gave 50.6% wet faeces at the same experimental condition. Further statistical analysis also showed that, the level of wet faeces produced by rats dosed with the root of this plant was significant ($p< 0.05$) as compared to the stem bark. Also, the stem bark and root of *C. sieberiana* exhibited 71% and 80% respectively of the potency of *S. alexandrina*. This difference in the investigated laxative activity of these plants could be as a result of the difference in the content of anthracene glycoside reported to be responsible for the laxative effect of *Cassia* and *Senna* species. The root of *C. sieberiana* could be used as a mild laxative (due to its lower content of anthracene glycoside) in patients such as pregnant women and children whom the *S. alexandrina* may be contraindicated due to its severe purgative action [37]

3.3. Antimicrobial activity

3.3.1. Antiviral activity

After decades of discovering the human immunodeficiency virus (HIV), there is still lack of curative therapy to curb this crux. Currently, medication for preventing mother to child transmission of HIV/AIDS, pre-exposure prophylaxis and post-exposure prophylaxis are available to prevent HIV/AIDS infection. Also, the availability of highly active anti-retroviral therapy (HAART) and anti-retroviral drugs (ARVS) which changes the HIV/AIDS from deadly into manageable chronic diseases. There still remain serious challenges such as cost, the undesirable side effects of these drugs, the long-term treatment and the lifelong adhesion [38]. The choice of therapy in the treatment of HIV/AIDS in developing countries is compromised due to limited healthcare capacities, persistent lack to ARVS, poverty etc. As a result, the use of traditional medicine is very common amongst people living with HIV infection in Africa [39,40]. Hence, it has become very necessary to study the efficacy of such plant preparation. The efficacy of *C. sieberiana* preparation in the treatment of HIV/AIDS has been investigated by MM Leteane and his team. The level of viral p24 antigen in infected peripheral blood mononuclear cells (PBMCs) and the cytopathic effect protection were measured by testing the inhibitory properties of the ethanolic tannin-free and tannin-containing extracts of the bark and root of *Cassia sieberiana*, against cloned HIV -1_C (MJ_4). The two extracts at a concentration of 150 µg/ml demonstrated inhibition in the production of p24 antigen in PBMCs seven days post infection with virally cloned cells; thus, the ethanol root extract of C. sieberiana showed a significant inhibition 98±3.1% ($p<0.05$) before and 94.5±10% ($p<0.05$) after the removal of the tannins. Also, the ethanol bark of the extract demonstrated an inhibition of 95±3.9% in the presence and 80±10% in the absence of tannins. The inhibitory activities of the tannin containing extracts could be as a result of the reported inhibitory properties targeting the formation of gp41 helix of HIV (Lü and his colleagues 2004), the binding of HIV gp120 to CD4 receptor [41] and HIV reverse transcriptase [42,43]. Also, the antiviral activity of the tannin free extracts may be as a result of the synergistic effect of the other phytochemical compounds or the activity of one constituent present via similar mechanism of action. The antiretroviral activity of *Cassia sieberiana* bark and root extracts was observed to occur in a concentrationdependent manner with effective concentration (EC_{50}) of 85.3 µg/ml and 65.1 µg/ml respectively. Further tests to determine its mechanism of action showed that, the bark and root extracts of the *Cassia sieberiana* blocked the replication of HIV -1_C at its entry (EC_{50} = 100.5 µg/ml and 88.9 µg/ml respectively) and binding stage (EC_{50} = 90.8 µg/ml and 70.2 µg/ml respectively). This shows that, the root bark and root extracts of this plant shows significant direct inhibitory activity against HIV -1_C replication [44]. The results from this study justifies its use in the treatment of HIV/AIDS patients infected by HIV -1_C in folk medicine.

3.3.2. Antibacterial activity

The evident emergence and spread of multidrug resistant bacterial in especially human population have become a major public health issue [45] This problem has called for the need in the continuous search for new safer, more effective and less expensive antibiotics. L. Traore and his team [46] investigated the antibacterial potential of the glycosidic and aglyconic crude extracts of the root bark of *Cassia sieberiana* against four (4) clinical isolates (*Vibrio cholerae, Salmonella sp, Proteus mirabilis and Shigella sp*) and three (3) reference strains (*Staphloccocus aureus* ATCC 25923, *Escherichia coli* ATCC 25922 *and Pseudomonas aeruginosa* ATCC 27853). The study

showed that, the zone of growth inhibition which ranged from 7.5 – 38 mm demonstrated a dose dependent response with the aglyconic crude extracts showing a more extensive zone of growth inhibition at the same concentration as the gylcosidic crude extract. The results of their study demonstrated that, the crude extracts possessed antibacterial activity (CMB/MIC ≤ 4) against the tested bacterial, except for *E. coli* and *P. aeruginosa* [47]. This could be as a result of the presence of secondary metabolites in the crude extract [48], [49]. However, the aglyconic crude extract demonstrated a more pronounced antibacterial activity as compared to the crude extract of the glycosides which confirms studies by Hassan and Mathesius [50]. The weak antibacterial activity of the glycosides may be due to the inhibition of its antibacterial activity by the glycones present and as a result, the release of the glycones from the glycosides via acid hydrolysis demonstrates the full antibacterial activity of the aglycones. Mshelia and his colleagues in their study also demonstrated that, the methanol and dichloromethane extracts of the root bark of *Cassia sieberiana* possess both bactericidal and bacteriostatic activity against *E. coli, Staph. aureus, P. aeruginosa and B. subtilis.* Their recorded zone of growth inhibition on the microorganisms by these extracts ranged from 2-20 mm at concentrations of 30, 25, 20 and 15 mg/ml [51]. Its reported anti-bacterial activity may be due to the presence of flavonoids, tannins and saponins. These phytochemical compounds acts by either altering the bacterial cell membrane, acts as an antimetabolite or inhibits the synthesis of nucleic acid, protein and /or cell wall [52]. The antibacterial activity demonstrated on both Gram (+) and Gram (-) bacterial shows that, *C. sieberiana* extract do not act on the bacterial cell wall but rather by an internal mechanism. Studies done by Ulanowska and his colleagues suggested that, its mechanism of action may be as a result of the action of the phytochemical compounds on the RNA, DNA and protein synthesis of the bacterial [53].

3.3.3. Anti-plasmodial activity

Malaria which is caused by *Plasmodium* species is a major public health issue. In 2017, out of a total of 219 million malaria cases reported in 87 countries, 92% of these cases were reported in African with reported 93% of malarial deaths [54]. The issue of insecticide resistance, drug resistance to most anti-malarials, war and civil distance, travel, population increase, environmental and climatic changes has made malaria the leading Africa‟s health problem. This has resulted in the continuous search for either natural or synthetic compounds for eradication of either the vector or the parasite for decades now [55]. Nuhu Abdulrazak and his team demonstrated the antiplasmodial activity of the ethanolic extracts of the stem bark and root of *Cassia sieberiana* in vivo. The team employed Peter‟s 4-day suppressive test against chloroquine sensitive *Plasmodium bergheri* (NK 65) infection in the swiss albino mice. The results showed a significant ($p < 0.05$) dose dependent reduction in the parasitaemia in *Plasmodium bergheri* mice treated with these extracts. Thus, for mice groups administered 100, 200 and 300 mg extract / kg body weight, the chemo suppression of the stem bark extract in level of parasitaemia were 17.6%, 38.0% and 69.9% respectively and that of the root extract were 30.7%, 52.7% and 55.8% respectively were recorded when compared to 96.0% suppressive rate obtained from weight of chloroquine. This study shows that, the root and stem bark of this plant can be explored for the treatment of malaria due to its anti-plasmodia activity [56]. This could be due to the presence of compounds such as alkaloids, flavonoids etc. For instance, terpenes, alkaloids, anthraquinones and flavonoids in plants have been indicated in antiplasmodial activities [57–59].

3.3.4. Anticoccidian activity

Coccidiosis, which causes mortality and results into significant financial loss to breeders is among the common chicken illnesses. Its treatment with veterinary medicine which is subject to resistance has raised major concerns with regards to their safety to consumers. This has necessitated the need to seek alternative source of treatment which is not only effective against this protozoan but also safe, cheap and readily accessible to farmers. Fall and his colleagues [60] investigated the anticoccidian activity of *Cassia sieberiana* because of its use in traditional medicine as an antiparasitic agent [61,62]. The anticoccidian activity of the ethanol root extract, the dichloromethane, ethyl acetate and methanol fractions of the root of *Cassia sieberiana* was investigated using the leghorn cobb 100 strain chicks who were experimentally infested via oral administration with *coccidia oocyst* (Eimeria spp). The parasitological examination aimed at determining the number of oocysts per gram of faeces (OPG) produced by infested chicks treated with the extract and fractions as well as those produced by infested chicks who were treated with amprolium (the reference product) was carried out. The result showed that, the ethanol root extract was more active than the amprolium, and the 3 fractions. Thus, at the end of treatment, the percentage of reduction in OPG in chicks treated with ethanol root extract (5 and 10 mg/day) were 74.39±6.81% and 88.63±7.89% respectively whereas the reference drug was only 58.42±5.78%. The reported low percentage in the reduction of OPG in experimental animals treated with amprolium could be as a result of chemoresistance of the coccidian against currently used medications for treatment of coccidiosis. This has been described in a study by [63]. Also, infested chicks treated with methanol fraction (7.225 mg/day) and those treated with dichloromethane fraction (0.131 mg/day) gave similar percentage reduction; thus 81.01±7.03% and 80.75 ± 7.25% respectively. Studies by Wink has described the triterpenoids [64] and polyphenols (flavonoids and tannins) [65] found in the roots of C. sieberiana to be responsible for its antiparasitic effect [66]. This study which also reported the absence of intestinal lesions in experimental animals treated with the extract and fractions could be as a result of the gastric cytoprotective properties of the phytochemical constituents in the plant [14]. This result justifies its use in Senegalese traditional medicine as antiparasitic agent [60].

3.4. Management of metabolic syndrome

This is a major public health problem worldwide affecting less than 10% to as much as 84% of the population depending on the composition (ethnicity, age, race and sex), the region, rural or urban environment of the studied population and the definition of the syndrome used [67,68]. Currently, pharmacological treatment involves the use of appropriate medication to treat the individual component of metabolic syndrome separately. Since many plants have been used in traditional medicine to treat such individual components, Nweje - Anyalowu and his team used suitable animal models which imitates all these symptoms of human metabolic syndrome to investigate the potential pharmacological use of the leaves of *Cassia sieberiana* in the management of hypertension, obesity, hypercholesterolemia, insulin resistance and other related components of metabolic syndrome which occur together increasing the risk of stroke, diabetes and heart diseases. In this study, forty (40) adult albino rats were randomly divided into 4 groups of 10 rats each. The first group was used as the control; thus, rats were fed with standard rat diet for 90 days. The second group were also fed with high fat diet (HFD) for 90 days. The third group were also fed HFD for 90 days but also given methanol leave extract of *Cassia sieberiana* (MECS) at 200 mg/kg/day from days 61-90 and finally the fourth group were concurrently fed with HFD and treated with MECS

(200 mg/kg/day) for 90 days. The effect of MECS treatment on some of the metabolic syndrome components were analysed via the measurement of the fasting blood sugar (FBS), triacylglyceride (TAG), body weight, serum insulin level, total cholesterol (T. Chol.), low density lipoprotein (LDL) and high-density lipoprotein (HDL) concentrations. The results demonstrated that, administration of MECS for 30 and 90 days reduced significantly ($p< 0.05$) the FBS, TAG, LDL, body weight and insulin level as well as a significant increase ($p< 0.05$) in the level of HDL in the serum. The reported reduction in serum cholesterol may be due to the levels of polyphenolic compounds present in the extract. Studies have also shown that, soluble dietary fibres in plants bind to dietary cholesterol and reduce or prevent its absorption by the small intestines [69,70]. Also, the decrease in serum TAG level by the extract may also be due to activities of the extract via an alteration in the level of interleukin-6 (IL-6) which mediates energy mobilization in the fat tissues and muscles [71] (serum TAG level is inversely proportional to the level of IL-6 and TNF-α, [72]). The increase in the level of serum HDL-C by the extract may be as a result of an increase in its biosynthesis by the liver due to flavonoids in the extract [73]. This will also result in an enhanced excretion of cholesterol as more will be transported from the peripheral tissues to the liver for excretion. The observed reduction in the levels of serum LDL-C may be as a result of the enhanced bile acid excretion and reverse transport of cholesterol via apo B production inhibition which is needed not only for LDL-C production but also for its transport and binding [74]. The anti-hyperglycaemic activity of the extract may be due to its relatively high antioxidant activity or via the release of insulin which inhibits the ATP-sensitive potassium channels in the membrane of residual beta-cells. There is also a possibility that, the extract might have enhanced insulin action to stimulate the uptake of glucose and its utilization by body tissues [75].

This demonstrate the possible protective effect of MECS against HFD induced metabolic syndrome in tested animals. However, further investigations need to be carried out to determine the various mechanisms of action [68].

4. Toxicity studies

The aqueous extract of *Cassia sieberiana* stem bark administered at 20, 60 or 180 mg/kg to rats for six weeks showed a 7% decrease in mean body weight gain and Significant ($p < 0.05$) increase in serum urea and creatinine concentrations with decrease in serum total protein concentrations in the group treated with the highest concentration (180 mg/kg) of the extract. Groups treated with the extract showed significant ($p < 0.05$) increase in serum ALT and AST activity, indicating that oral administration of aqueous extract of *C. sieberiana* stem bark result in hepatotoxicity even at lower doses and nephrotoxicity at higher dose of 180 mg/kg [76]. The acute toxicity study of the pods (fruit) extract showed LD_{50} value of 1950 mg/kg, with significant ($P<0.05$) elevation of serum levels of ALT (1600mg/kg treated group), ALP (400, 800 and 1600mg/kg treated groups), and AST (all the treated group) when compared to the control group. Even though the calculated LD50 of fruit extract indicated a low toxicity, the study showed that prolong use of the extract at a high dose (400–1600 mg/kg) can cause liver damage [9]. Acute toxicity of root bark extract (5–2000 mg/kg, p.o) given as a single dose showed no signs of acute toxicity. No mortality was recorded when animals were observed for 14 days after administering extract [14]. The single dose oral administration of 5000 mg/kg of aqueous root bark extract of *Cassia Sieberiana* to animals did not result in death (LD_{50} >5000 mg/kg) and there were no significant differences ($p>0.05$) between the haematological study of the test animals and that of the control animals. Also, the albumin, alkaline phosphatase

and total bilirubin were significantly ($p<0.05$) higher in the test animals when compared to the controls. Liver micrographs after sub-chronic studies showed centrilobular necrosis at the dose of 750 mg/kg, indicating toxic effects of the extract on the liver at high doses on prolonged administration [77]. Ajayi and his colleagues [78] also reported the lethal oral dose (LD_{50}) for hot infusion of *C. sieberiana* to be >5000 mg/kg in rats, with the rats treated with 500 and 1000 mg/kg of the *C. sieberiana* extract showing a reversible proliferation of the messenchyma cells of the kidney, mild periportal infiltration of the liver and mild to moderate testicular atrophy in histo-pathological examination. Hydro-alcoholic root extract of *C. sieberiana* when administered to rats during acute and sub-chronic toxicity studies resulted in no death with no signs of toxicity. However, the histological study, after 28 days of administration (sub-chronic), revealed necrotic and inflammatory cells in the hepatic parenchyma and a sinusoidal stasis. The extract again seems to be cytotoxic, on cell viability, at very high doses [79]. The acute toxicity study of aqueous extract of *Cassia sieberiana* by Tamboura and his team [80], also showed that LD_{50} of 24 mg/kg. The oral administration of 400 and 800 mg/kg *C. sieberiana* aqueous stem bark extract caused significant ($P<0.05$) increase in AST, ALT, ALP, decrease in total protein, albumin and body weight. The 400 and 800 mg/kg treated rats H and E stained liver sections revealed significant hepatocellular changes, with lymphocytic and neutrophilic infiltrations as well as mild focal necrosis, observed around perivenular region, indicating hepatotoxicity of the extract at high dose levels and prolonged administration. However, when treatment was stopped for some period, biochemical changes were reversed, indicating recovery after withdrawal of treatment [81]. *Cassia sieberiana* aqueous leaf extract when administered to rats produced immediate clinical signs such as weakness, depression, starry hair coat, anorexia. Also, abnormal gait, lordosis, ophthalmia, coma and death appeared after 2 hours, with calculated median lethal dose (LD_{50}) of 960 mg/kg. Hepatomegaly, focal necrosis, sinusoidal congestion with periportal necrosis, Kupffer cell proliferation, enlargement of the kidneys, vascular degeneration and interstitial mononuclear cell infiltration were observed during tissue and organs examination [82]. These toxicity studies suggest that *Cassia sieberiana* may be toxic at higher doses and prolonged usage, therefore caution must be taken as to how to use it.

5. Conclusion

This review has shown that *cassia sieberiana* has numerous medicinal properties; thus, there are reasonable number of researches to back its documented use in traditional medicine. This could be a source of new compounds which may be more effective, less toxic and less expensive for drug formulation and treatment of certain prevalent diseases of public health interest.

6. Recommendation

The need for more research into bioassay guided isolation and purification of extracts to determine the exact phytoconstituents responsible for its various activities.

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