



Holarrhena floribunda: A Potential Traditional Plant

Aseem Setia^{1*}, Manmohan S. Jangdey¹, Mrinal Sharma², Pradeep Golani³, Mayur Bhurat⁴, Amit Kumar Dhankani⁵, Sanjay Nagdev⁴, Gaurav Mude⁴

¹Department of Pharmacy, Shri Rawatpura Sarkar University, Raipur, (C.G) -492015, India

²Sachdeva College of Pharmacy, Gharuan- 140413, Chandigarh (Punjab), India

³Department of Pharmacy, Gyan Ganga Institute of Technology and Sciences, Jabalpur- 482003 (M.P.), India

⁴Shri. Prakashchand Jain College of Pharmacy and Research, Palaskhede (Bk.), Jamner- 424206 (Maharashtra), India

⁵P.S.G.V.P.M's College of Pharmacy, Shahada, Nandurbar-425409, Maharashtra, India

ABSTRACT

A wide spectrum of traditional medical methods employs *Holarrhena floribunda* (HF). A major source of novel pharmaceutically active compounds has always been plants. When it comes to treating disorders that do not respond well to synthetic medications, the modern medical system offers a wide range of herbal choices. There are a number of plants that have been used as medicine from ancient times to heal illnesses. Medicinal properties of herbal plants can be found in their chemical components. It is widely used in Togolese folk medicine as *Holarrhena floribunda*. False rubber tree, *Holarrhena floribunda*, belongs to the Apocynaceae family and may reach a height of 17 metres. Many components of the plant are used medicinally in West Africa. This plant has a variety of chemical components that are used to cure malaria, amoebic illness, diarrhoea, fever, infertility, and diabetes through the usage of plant parts including stem bark and leaves. In addition to highlighting *Holarrhena floribunda*'s chemical composition, this paper also examines the plant's pharmacological properties.

Keywords: Chemical constituent, Pharmacological activities, *Holarrhena floribunda*

Article History:

Received: 26 May 2021

Revised: 30 Aug 2021

Accepted: 30 Aug 2021

Published: 31 Aug 2021

Corresponding Author:

Aseem Setia, Department of Pharmacy, Shri Rawatpura Sarkar University, Raipur, (C.G) -492015, India

Email: aseemsetia77@gmail.com

Mobile: +919098070535

INTRODUCTION

Traditionally throughout Africa, *Holarrhena floribunda* has been used to cure a wide range of ailments, including diarrhoea, sterility, and diabetes¹. It is a 17-meter-tall tree with a 1-meter-wide trunk found in deciduous forest and savanna woodland. Follicles are up to 60 cm long and fruit is pale grey to dark brown². Senegal, Nigeria, and other regions of West Africa are known to harbour it. As time goes on, the use of herbal plants in the current medical system will become more common place. There aren't a lot of alternatives when it comes to medicines.

Holarrhena floribunda is a member of the Apocynaceae family and contains a number of useful phytochemicals that have been shown to have health benefits, the description of plant parts given in (Table 1). Rubber tree is the common name for *Holarrhena floribunda*, sometimes known as false rubber tree³. This plant has a variety of chemical components that are used to cure malaria, amoebic illness, diarrhoea, fever, infertility, and diabetes through the usage of plant parts including stem bark and leaves. Snakebites and venereal illnesses were treated with the boiling milk with the roots. As a result, the tree

produces a lot of alkaloids. The roots contain the most alkaloids (2%) followed by the stem (1-1.5%) and the leaves (< 1.0%)⁴. As an anti-malarial, the leaves of this plant have been used for centuries. Leaf and bark are used to treat diarrhoea in Ivory Coast, whereas the leaves alone are used to treat amenorrhea and diabetes⁵.

Table 1: Plant *Holarrhena floribunda* different parts description

Plant Part	Description
Leaves	Shape is ovate-acuminate or lanceolate, shiny, 2-8 cm broad and 5-18 cm long
Flowers	Scented, white, in umbel-like inflorescences
Fruits	Narrowly Paired, cylindrical fruting follicles

Despite the fact that the leaves of this plant have been used in folk medicine to treat a variety of diseases, little is known about the phytochemicals present in the plant, and thus the relevance of the antioxidant properties of this plant⁶. Chemical compounds in plants have therapeutic relevance because they have a specific physiological effect on the human body. Due to the presence of phytochemical components, medicinal plants are beneficial for treating and curing human illnesses. Alkaloids, tannins, flavonoids, and phenolic chemicals are the most significant bioactive components of plants⁷. As a result, many of the native medicines are also utilised as spices or food plants. As a result, they are occasionally added to pregnant women's and nursing mothers' meals for therapeutic purposes.

Traditional healers have utilised different portions of the *Holarrhena floribunda* to cure a variety of illnesses and diseases. This plant is used to cure boils, eczema, and diabetes mellitus in northern Nigeria using decoctions of the dried leaves⁸. Headaches can be relieved by applying crushed leaves to the forehead. For stimulant, carminative, diuretic and antipyretic purposes, leaves and inflorescence are infused⁹. In this article, we've tried to cover all of the known pharmacological properties,

such as anti-cancer, analgesic, anti-malarial, hypoglycemic activity, antioxidant activity, and antibacterial activity, among others. As well as discussing different features of the plant *Holarrhena floribunda*, this article emphasizes the plant's prospective benefits. Plants that contain bioactive polyphenolics have been extracted and identified by Badmus et al. (2016). *Holarrhena floribunda* yielded three recognised flavonoids (Fig 1): Kaemperol-3-O rutinoside, quercetin-3-O-glucoside, and kaemperol-3-O-glucose, as well as a 1:1 combination of quercetin-3-O-glucose/galactose¹⁰.

TRADITIONAL USES OF *HOLARRHENA floribunda*

It has been claimed that *holarrhena floribunda* has therapeutic potential in all of its components¹¹. Because of their unparalleled chemical variety, plants are a goldmine for novel therapeutic leads. The biological characteristics of this plant, on the other hand, have been the subject of very few experimental researches. Because it inhibited drug-resistant strains of *Plasmodium falciparum*, the stem bark of *H. floribunda* might be used as a quinine replacement¹².

There's also conessine, which is used to destroy amoeba without having an emetic impact. Tonics, snake bite remedies, and venereal illnesses and dysentery are all treated using the stem bark. The bark is used to alleviate stomach discomfort, nausea, indigestion, and diarrhoea in various regions of West Africa¹³. It is used to treat constipation, colic, and sterility. Diarrhea and dysentery are also treated with this drug. In addition, the root is boiled in milk and used to bath boys attaining puberty, the root is also used to treat snakebites and venereal illness. In the past, the leaves of *H. floribunda* were used to cure malaria, dysentery, diarrhoea, amenorrhea, and to control diabetic symptoms. It is used as an enema to treat kidney discomfort when combined with *Myrianthus arboreus* and *Capsicum* fruits¹⁴.

To cure gonorrhoea in Sierra Leone, the leaves are combined with kola nuts and consumed. As a hemostatic, the leaf sap is applied to wounds. A cure for dropsy is made from the fruit in Guinea Bissau (Guinea Bissau). The latex is used to treat snakebites and stings (Table 2).

PHYTOCHEMICAL AND ISOLATED COMPOUND OF *HOLARRHENA floribunda*

Holaphylline and holaphyllamine were discovered as a result of a chemical analysis of the leaves of *Holarrhena floribunda* (H.F)¹⁵. Figure 2 displays the structures of holaphylline, holaphyllamine,

conessine and progesterone, which were isolated from *H. floribunda*. Using a plant extract from *Holarrhena floribunda* stems, Loukaci and coworkers isolated novel trichothecenes, 8-dihydrotrichothecinol, loukacinol A, loukacinol B and trichothecin as well as recognised chemicals trichothecolone and trichothecinol A, rosenonolactone and 6 α -hydroxyrosenonolactone¹⁶.

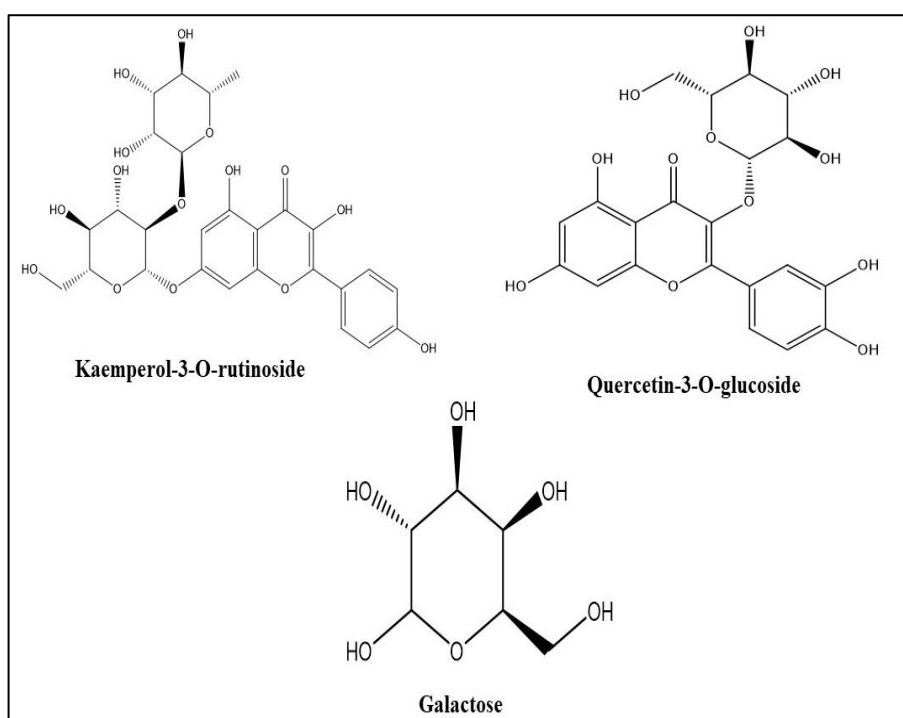
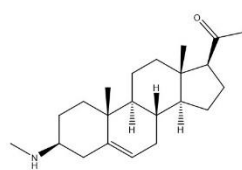
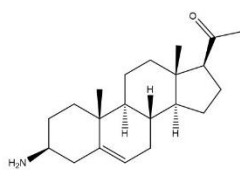
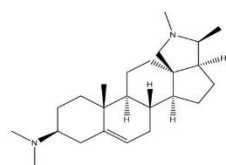
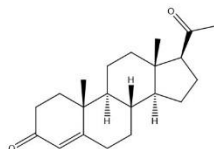
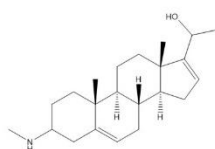
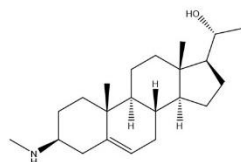
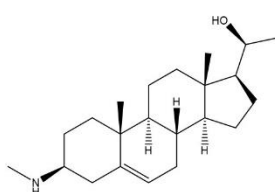
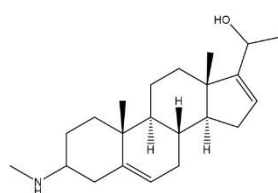
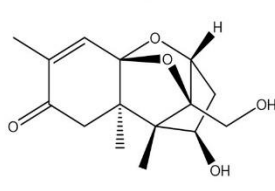
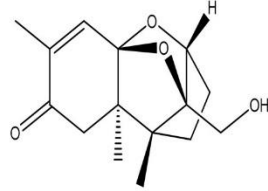
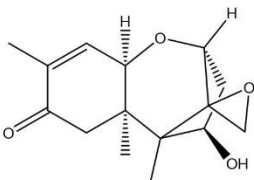
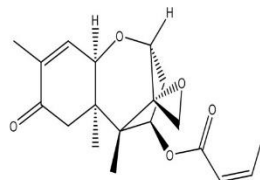


Fig 1: Flavonoids isolated from *H. floribunda*

Table 2: Chemical Constituents present in different parts of *Holarrhena floribunda*

Plant part	Chemical Constituents
Stem	Trichothecenes, trichothecolone, rosenonolactone, 8-dihydrotrichothecinol.
Bark	Conessine, alkaloids, lupeol and its three long-chain fatty acid ester derivatives.
Root	Conessine
Leaves	Flavonoids (Kaemperol-3-O-rutinoside, quercetin-3-O-glucoside & kaemperol-3-O-glucoside), holaphylline, holamine, progesterone.

**Holaphylline****Holaphyllamine****Conessine****Progesterone****Holadysamine****Holaphyllinol****Holaphyllidine****Holadysamine****Loukacinol A****Loukacinol B****Trichothecolone****Trichothecin****Fig 2: Chemical compounds isolated from *Holarrhena floribunda***

PHARMACOLOGICAL AND BIOLOGICAL ACTIVITIES

Badmus et al; 2015 investigated the antiproliferative and apoptosis induction potential of methanolic leaf extracts of HF against breast (MCF-7), colorectal (HT-29), and cervical (HeLa) cancer cells relative to normal KMST-6 fibroblasts. The extract's dose-response studies revealed that cancer cell lines were more sensitive to the extract than fibroblasts. For the cancer cell lines examined, the induction of apoptosis, ROS, and cell cycle arrest was time- and dose-dependent. As a result of these findings, further research into the isolation, characterisation, and mechanistic assessment of the bioactive chemicals responsible for the antiproliferative action of the plant extract will be undertaken¹⁷. Yemoa et al; 2015 tested hydroethanolic extracts from the aerial portions of *Holarrhena floribunda* (G. Don) T. Durand and Schinz against *M. ulcerans* (MIC = 125 $\mu\text{g/mL}$), they observed considerable antimycobacterial activity. There was enough pure holadysamine available to determine its MCI (=50 $\mu\text{g/mL}$). These findings provide credence to the historic usage of this herb in medicine¹⁸.

Hoekou et al; 2017 investigated the antimicrobial activity of *Holarrhena floribunda* using ethanolic extract. *Staphylococcus aureus* ATCC 29213 and clinical strains of *Staphylococcus aureus*, *Salmonella typhi*, and *Klebsiella pneumoniae* were all susceptible to the ethanolic extract of *H. floribunda* leaves, which had MICs ranging from 0.62 to 1.25 mg/mL. Parasitaemia was also suppressed by the extract in a dose-dependent fashion. Toxicologically, the extract administered to mice did not change the relative weight of important organs, and there were no symptoms of toxicity or mortality during the research. In the test, the extract's LD50 was determined to be more than 5,000 mg/kg, suggesting that it was safe to consume. This study reveals the antibacterial and antimalarial properties of *H. floribunda* leaves, and thus supports its therapeutic application in the treatment of microbial diseases, according to the authors¹⁹. Nnadi et al; 2017 investigated extracts from the leaves and bark of the West African *Holarrhena africana*. Against *T. brucei rhodesiense* bloodstream forms, the extracts and their alkaloid-enriched fractions showed good in vitro activity (Tbr; East African HAT). It was possible to isolate 17 steroid alkaloids, one nitrogenless steroid, and one

non-steroid alkaloid by bioactivity-guided fractionation of alkaloid-rich fractions. Impressive activities (IC₅₀ in μM) against Tbr were recorded for 3 β -holaphyllamine (0.40 ± 0.28), 3 α -holaphyllamine (0.37 ± 0.16), 3 β -dihydroholaphyllamine (0.67 ± 0.03), N-methylholaphyllamine (0.08 ± 0.01), conessimine (0.17 ± 0.08), conessine (0.42 ± 0.09), isoconessimine (0.17 ± 0.11) and holarrhesine (0.12 ± 0.08) with selectivity indices ranging from 13 to 302²⁰.

Kpegba et al; 2018 investigated the antioxidant activity using hydro-ethanolic extract of the trunk bark via the DPPH radical-scavenging and the ferric-reducing antioxidant power (FRAP) methods, and via the determination of the total phenolics content. To test the effects of plant extracts on blood pressure in sound guinea pigs, this hydro-ethanolic extract was employed. *Floribunda* has the majority of phytochemical groups, according to phytochemical screening. The extract's 50% inhibitory concentration was $29.80 \pm 0.001 \mu\text{g/mL}$. In dry extract, FRAP measured Fe²⁺ equivalents of $1009.9 \pm 0.6 \mu\text{mol/g}$. The dried extract contained $139 \pm 0.053 \text{ mg GAE (gallic acid equivalents)/g}$ of phenolic components. By injecting the extract (10, 20, 40 and 80 mg/kg) intravenously into normal-stressed Guinea pigs, it reduced diastolic blood pressure, as well as the systolic blood pressure and the mean arterial pressure (MAP) on a dose- and time-dependent basis. Hydro-ethanolic extract of *H. floribunda* trunk bark exhibits antihypertensive and antioxidant activities, according to the results of the study. This might be the rationale for the usage of that extract in traditional medicine to treat high blood pressure²¹.

Anti-Diarrheal Activity

Aska et al; 2010 investigated the aqueous extract of leaves of *Holarrhena floribunda* for anti-diarrheal activity by castor oil induced diarrhea, intestinal secretion and small intestine charcoal meal transit in rats. The results showed significant reduction in charcoal meal transit and secretary associated diarrhea²².

Anti-Bacterial Activity

Patrice et al; 2007 evaluated the methanolic extract of stem bark of plant *Holarrhena floribunda* and isolated conessine on different types of micro-organisms by disc diffusion method. The results

suggested showed a significant antibacterial effect against all the strains⁷.

Anti-Malarial Activity

Fotei et al; 2006 from the ethno-pharmacological investigation found that *Holarrhena floribunda* stem bark is used in daily life for its anti-malarial activity. They examined different extracts activity on the different strains with the help of *in vitro* method and bioassay. The results showed that ethanolic, aqueous and chloroform extracts of stem bark non alkaloid fraction showed activity against *Plasmodium falciparum*, when tested *in vitro* the aqueous extract and ethanolic extract showed the activity against two strains. So, the results suggested good antimalarial activity of the plant²³.

Antimicrobial Activity

Hoekou et al; 2017 investigated the ethanolic extract of leaves of *Holarrhena floribunda* for the antimicrobial activity. The antimicrobial activity was examined with the help of agar well-diffusion method. The results showed that extract was active against many clinical strains and suggested good antimicrobial activity¹⁹.

Anti-Mycobacterial Activity

Yemoa et al; 2015 examined different plant used in Benin for the BU (Buruli ulcer) and investigated them for their anti-mycobacterial activity. Crude hydroethanolic extract from aerial parts of *Holarrhena floribunda* showed significant results in the inhibition of *Mycobacterium ulcerans* and purified holadysamine chemical constituent for the particular inhibition¹⁸.

Antioxidant, Anti-Mutagenic Activity

Badmus et al; 2013 evaluated the antioxidant and anti-mutagenic activities of ethyl acetate, aqueous and methanolic extracts of leaves of *Holarrhena floribunda*. Ethyl acetate fraction showed stronger activity than other. All the fractions showed Anti-mutagenic activity against cyclophosphamide induced chromosomal aberrations²⁴.

Anti-Cancer Activity

Badmus et al; 2015 examined methanolic leaf extract of *Holarrhena floribunda* against breast (MCF-7), colorectal (HT-29) and cervical (HeLa) cancer cells

relative to normal KMST-6 fibroblasts. Results showed induction of apoptosis, ROS, and cell arrest were dose and time dependent¹⁷. Badmus et al; 2019 isolated compounds from the leaves of *Holarrhena floribunda* using bioassay guided fractionation and the step wise application of the MTT reduction assay to access anti-proliferative bioactivity. Isolated compounds showed significant results in the cytotoxicity against the cancer cell lines²⁵.

Hypoglycaemic Activity

Gnangoran et al; 2012 examined leaf ethanolic extract and various fractions of this extract of *Holarrhena floribunda*. The extract showed significant down regulation of blood glucose, reduced or totally prevented the induction of hyperglycemia. The results showed that leaves of plant ethyl acetate and dichloromethane extract showed good hypoglycemic activity⁶.

Sex Hormones And Sterility/Fertility Treatment

Ekpe et al; 2019 studied methanolic extract of root of *Holarrhena floribunda* on female Wistar rats for liver enzymes effect and histopathology of ovaries and testes tissues of the rats. The results showed that extract has no toxic effect on liver and in ovaries and testes tissues no disorganization and degeneration seen. The results suggested its activity for the sterility/fertility disorders in women [26]. Dennis et al; 2018 studied methanolic root extract of *Holarrhena floribunda* for its lipid profile & sex hormones level in male and female wistar rats. The results showed improvement in the serum level of sex hormones in male as well as female rats and showed enhanced reproductive functions²⁷.

Analgesic Activity

Aniefiok et al; 2014 evaluated the analgesic activity of methanol root extract of *Holarrhena floribunda* using thermally induced pains, acetic acid induced writhing and formalin-hind paw licking in mice models. The extract showed significant analgesic effect in all the models²⁸.

Toxicity

Bogne et al; 2012 investigated the Acute and sub-acute toxicity of the methanol extracts from *Holarrhena floribunda* G. Don. The results showed

that moderate intake of the plant extract up to 1g/kg has no toxic effect while high intake up to 2g/kg was toxic. According to Koudou et al., 2017 administration of *Holarrhena floribunda* in wistar rats did not result in functional disturbances or cardiac damage in rats²⁹.

CONCLUSION

A variety of active phytochemical components are present in *Holarrhena floribunda*, which may be responsible for the plant's numerous therapeutic applications and pharmacological activity. A lot of more research has to be done on *Holarrhena floribunda* if it is to be confirmed as a therapeutic plant. To assist researchers and scientists better understand the characteristics of *Holarrhena floribunda*, this article contains useful information about the plant.

CONFLICT OF INTEREST

None

AUTHORS' CONTRIBUTIONS

AS, MSJ, MS, AKD, MB, SN, PG, GM

AS: Literature review, Writing original draft- review & editing; MS: Conceptualization, Supervision, Writing- review & editing; MSJ, AKD & MB: Data collection, Tabular arrangement, Writing- review & editing; SN and PG: Data collection, Writing- review & editing; GM: Data collection, Creating figures, Writing- review & editing; The final manuscript was reviewed and approved by all of the authors.

REFERENCES

1. Hoekou YP, Tchacondo T, Karou SD, Yerbanga RS, Achoribo E, Da O, Atakpama W, Batawila K. Therapeutic potentials of ethanolic extract of leaves of *Holarrhena floribunda* (G. Don) Dur. and schinz (apocynaceae). African Journal of Traditional, Complementary and Alternative Medicines. 2017; 14(2): 227-33.
2. Dennis A, Udosen EO, Ekam VS, Ekpe IP. Effects of methanolic root extract of *Holarrhena floribunda* on the Lipid Profile and Sex Hormones in Wistar Rats. Asian Journal of Research in Biochemistry. 2018: 1-7.

3. Onefeli AO, Kehinde LP. Taxonomic Value of Leaf Epidermal Markers in Discriminating Some Medicinal Tree Species of Apocynaceae Juss. In Environmental Sciences Proceedings. 2020; 3 (1): 91.
4. Tamboura HH, Bayala B, Lompo M, Guissoe IP, Sawadogo L. Ecological distribution, morphological characteristics and acute toxicity of aqueous extracts of *holarrhena floribunda* (g. don) durand & schinz, *leptadenia hastata* (pers.) decne and *cassia sieberiana* (dc) used by veterinary healers in burkina faso. african journal of traditional, complementary and alternative medicines. 2005; 2(1): 13-24.
5. Titanji VP, Zofou D, Ngemenya MN. The antimalarial potential of medicinal plants used for the treatment of malaria in Cameroonian folk medicine. African journal of traditional, complementary, and alternative medicines. 2008; 5(3): 302.
6. Gngorran BN, N'guessan BB, Amoateng P, Dosso K, Yapo AP, Ehile EE. Hypoglycaemic activity of ethanolic leaf extract and fractions of *Holarrhena floribunda* (Apocynaceae). Journal of Medical and Biomedical Sciences. 2012; 1(3): 46-54.
7. Patrice KM, Véronique PB, David L, François-Xavier E. Antibacterial activities of the extracts and conessine from *Holarrhena floribunda* G. Don.(Apocynaceae). African Journal of Traditional, Complementary and Alternative Medicines. 2007; 4(3): 352-6.
8. EL-Kamali HH. Medicinal plants in east and central Africa: challenges and constraints. Ethnobotanical Leaflets. 2009; 2009(2): 12.
9. Bhusal A, Jamarkattel N, Shrestha A, Lamsal NK, Shakya S, Rajbhandari S. Evaluation of antioxidative and antidiabetic activity of bark of *Holarrhena pubescens* wall. Journal of clinical and diagnostic research: JCDR. 2014; 8(9): HC05.
10. Badmus JA, Ekpo OE, Rautenbach F, Marnewick JL, Hussein AA, Hiss DC. Isolation and antioxidant activity of flavonoids from *Holarrhena floribunda* (G. don) leaves. Acta Biochimica Polonica. 2016; 63(2): 353-8.
11. Zahara K, Panda SK, Swain SS, Luyten W. Metabolic Diversity and Therapeutic Potential of *Holarrhena pubescens*: An Important Ethnomedicinal Plant. Biomolecules. 2020; 10(9): 1341.
12. Fotie J, Bohle DS, Leimanis ML, Georges E, Rukunga G, Nkengfack AE. Lupeol Long-Chain Fatty Acid Esters with Antimalarial Activity from *Holarrhena floribunda*. Journal of Natural Products. 2006; 69(1): 62-7.
13. Udoh AE, Nwafor PA, Udobre AS. The Antidiarrheal Activities of Methanol extract of *Holarrhena Floribunda* on rodents. Nigerian Journal of Pharmaceutical and Applied Science Research. 2011; 1(2): 67-73.
14. Ahmed H. A phyto pharmacological review on a medicinal plant: *Holarrhena floribunda*. Journal of Medicinal Plants Studies. 2017; 5(6): 26-9.
15. Zahid A, Jaber R, Laggoun F, Lehner A, Remy-Jouet I, Pamard O, Beaupierre S, Leprince J, Follet-Gueye ML, Vicié-Gibouin M, Latour X. Holaphyllamine, a steroid, is able to induce defense responses in *Arabidopsis thaliana* and increases resistance against bacterial infection. Planta. 2017; 246(6): 1109-24.
16. Loukaci A, Kayser O, Bindseil KU, Siems K, Frevert J, Abreu PM. New Trichothecenes Isolated from *Holarrhena floribunda*. Journal of natural products. 2000; 63(1): 52-6.
17. Badmus JA, Ekpo OE, Hussein AA, Meyer M, Hiss DC. Antiproliferative and apoptosis induction potential of the methanolic leaf extract of *Holarrhena floribunda* (G. Don). Evidence-Based Complementary and Alternative Medicine. 2015.
18. Yemoa A, Gbenou J, Affolabi D, Moudachirou M, Bigot A, Anagonou S, Portaels F, Martin A, Quetin-Leclercq J. Beninese medicinal plants as a source of antimycobacterial agents: bioguided fractionation and in vitro activity of alkaloids isolated from *Holarrhena floribunda* used in traditional treatment of buruli ulcer. BioMed Research International. 2015.
19. Hoekou YP, Tchacondo T, Karou SD, Yerbanga RS, Achoribo E, Da O, Atakpama W, Batawila K.

- Therapeutic potentials of ethanolic extract of leaves of *Holarrhena floribunda* (G. Don) Dur. and schinz (apocynaceae). *African Journal of Traditional, Complementary and Alternative Medicines*. 2017; 14(2): 227-33.
20. Nnadi CO, Nwodo NJ, Kaiser M, Brun R, Schmidt TJ. Steroid Alkaloids from *Holarrhena africana* with Strong Activity against *Trypanosoma brucei rhodesiense*. *Molecules*. 2017; 22(7): 1129.
 21. Kpegba K, Tété Kondo E, Simalou O, Togbenou K, Boyode P, Toundou O, Gbandjaba Y, Agbonon A, Gbeassor M. A significant antihypertensive effect of *Holarrhena floribunda* supported by an exploratory phytochemical study. *Journal of Herbmmed Pharmacology*. 2018; 7(3).
 22. Aska AS, Pindiga YN, Abdulrahman FI, da Silva JA, Buratai LB. Anti-Diarrheal Effects of Aqueous Leaf Extract of *Holarrhena floribunda* (G. Don) Schinz and Dur in Rats. *Medicinal and Aromatic Plant Science and Biotechnology*. 2010; 4(1): 52-4.
 23. Fotie J, Bohle DS, Leimanis ML, Georges E, Rukunga G, Nkengfack AE. Lupeol Long-Chain Fatty Acid Esters with Antimalarial Activity from *Holarrhena floribunda*. *Journal of Natural Products*. 2006; 69(1): 62-7.
 24. Badmus JA, Odunola OA, Yekeen TA, Gbadegesin AM, Fatoki JO, Godo MO, Oyebanjo KS, Hiss DC. Evaluation of antioxidant, antimutagenic, and lipid peroxidation inhibitory activities of selected fractions of *Holarrhena floribunda* (G. Don) leaves. *Acta Biochimica Polonica*. 2013 Aug 1;60(3).
 25. Badmus JA, Ekpo OE, Hussein AA, Meyer M, Hiss DC. Cytotoxic and cell cycle arrest properties of two steroidal alkaloids isolated from *Holarrhena floribunda* (G. Don) T. Durand & Schinz leaves. *BMC complementary and alternative medicine*. 2019; 19(1): 1-9.
 26. Ekpe IP, Yisa BN. Effects of Methanolic Root Extract of *Holarrhena floribunda* on Liver Enzymes and Histopathology of the Ovaries and testes Tissues in Wistar Rats. *Asian Journal of Research and Reports in Endocrinology*. 2019; 20: 1-7.
 27. Dennis A, Udosen EO, Ekam VS, Ekpe IP. Effects of methanolic root extract of *Holarrhena floribunda* on the Lipid Profile and Sex Hormones in Wistar Rats. *Asian Journal of Research in Biochemistry*. 2018:1-7.
 28. Aniefiok Udobre, Udoh AE, Nwafor PA. Effect of the Methanol Root Extract Of *Holarrhena Floribunda* In Albino Mice, *Indo American Journal of Pharmaceutical Research*. 2014; 4(1), 148-153.
 29. Bogne KP, Penlap BV, Mbofung CM, Etoa FX. Acute And Subacute Toxicity Of The Methanol Extract From *Holarrhena Floribunda* G. Don (Apocynaceae). *European Journal of Experimental Biology*, 2012; 2(4): 1284-1288.