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Review Article

Review on Phytochemistry of Medicinal Plants Documented for the Treatment of Low Sperm Count in Oluponna, Nigeria

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ABSTRACT

According to the literature, approximately 32% of adult males in developing countries suffer from infertility, however, majority of them use herbal remedies with reported benefits such as improved sperm quality, sexual functions, libido and testosterone levels. Recently, the World Health Organization emphasized the importance of documenting active medicinal plants used in various continents. Therefore, this present review focused on the phytochemistry of medicinal plants reported for the treatment of low sperm count in Oluponna area of Osun state, documented in an ancestral local record. Thirteen medicinal plants were documented to be used for management of low sperm count among men in this community. The plants listed in the document belong to ten families and 12 genera. The most cited family in this record is Apocynaceae with three species of plants namely, *Alstonia boonei*, *Laidolphia dulcis*, and *Rauwolfia vomitoria* respectively. Since this is the first review on the documentation of an ancestral knowledge and application of medicinal plants as means of passing the knowledge from a generation to another in Oluponna, additional toxicological and pharmacological studies are hereby recommended in order to provide scientific rationale for the long-term knowledge and use of these plants.

Key words: Ancestral medicinal plants records, Low sperm count, Phytochemistry, Infertility, Drug development.

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INTRODUCTION

Infertility is one of the most serious problems that some people face around the world, and men account for half of all infertility cases.[1] The cause of almost 40% of the 2.1 million infertile young married couples in the United States is male infertility.[2,3] This issue is identified in approximately one out of every thirteen couples attempting to conceive.[4] Infertility can be caused by androgen deficiency or a low testosterone level, according to the United States Food and Drug Administration (FDA). Testosterone deficiency in men can cause symptoms such as decreased libido and erectile quality, low or no sperm count in sperm, decreased body hair, decreased lean body mass, and mood changes.[5] The history, physical examination, and, of course, sperm analysis can all be used to perform diagnostic testing.[4] Infertility evaluation can help determine the underlying cause of infertility as well as provide treatment to allow conception to occur.[6]

Oligozoospermia or azoospermia were present in 45 percent of infertile males in a multicenter World Health Organization study.[7] According to Stephen and Chandra (2006),[8] azoospermia affects 1 percent of men's population and between 10 and 15 percent of men who are infertile worldwide.[9] The prevalence of azoospermia and oligozoospermia among the married men from various regions of India varies by region. Kurnool and Jodhpur have a greater prevalence of azoospermia than any other place in the globe.[10] This can be because there are high levels of tobacco product consumption in this region.[3] In Africa, male infertility affects up to 32% of men.[3] For instance, a study on 661 male partners of infertile couples at the Obafemi Awolowo University Teaching Hospital in Ile-Ife, Nigeria, which was conducted in Fertility and Endocrinology Research Unit, revealed oligozoospermia, teratozoospermia, asthenozoospermia, azoospermia, oligoteratozoospermia and oligoasthenozoospermia in 25.6%, 18.5%, 11.5%, 6.2%, 3.2%, 2.3%, 2.1%, and 0.9%, respectively of participants.[11]

According to Schulte et al. (2010),[12] assessing sperm characteristics is becoming increasingly important in reproductive studies. When clinical complaints are accompanied by a decrease in testosterone, the doctor will begin Testosterone Replacement Therapy (TRT). However, if TRT is used excessively, side effects may occur. Nausea, acne, headache, fluid retention, liver toxicity, sleep apnea, tender breasts, polycytemia, and prostate hyperplasia are a few examples.[4,13] Due to the various side effects of hormone therapy, herbal medicines have gained widespread acceptance in recent decades.

Traditional medicines continue to play an important role in the healthcare systems of many people around the world, including Indians, Chinese, Africans, Americans, and others.[14-16] The World Health Organization recently emphasized the importance of documenting active medicinal plants used on various continents.[17] Even in the United States, a National Center for Complementary and Alternative Medicine has been established.[18] In most developing nations, men with infertility cases frequently use herbal remedies, with reported benefits including improved sperm quality, sexual functions, libido and testosterone levels.[19-23] For this reason, numerous plants with aphrodisiac and beneficial testicular effects (such as sperm counts, motility and viability), which are of great significance in our social lives,

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have been screened for male fertility boosting effects in many countries around the world, though dearth of systematic data on the molecular basis of these effects on the gonads existed. Infertile couples in the majority of emerging nations seek therapy using both traditional remedies and cutting-edge procedures.

Traditional medicine remains the common primary treatment option for infertile couples in underdeveloped nations due to limited access to orthodox treatments.[24] Consequently, even though many medicinal plants or natural products lack scientific backing, the use of herbal treatments, particularly in rural regions of developing and underdeveloped countries, continues to increase. Infertility issues are empirically treated with extracts, decoctions, or compounds isolated from medicinal plants. These herbal treatments are used to treat erectile dysfunction, sperm production defects (azoospermia, oligospermia), sexual weakness and diminished libido.[25] Therefore, the goal of this review was to compile information on the phytochemistry of medicinal plants documented in Oluponna for treating male infertility over the years.

MATERIALS AND METHODS

Cross-examination of documented plants

Oluponna (Latitude: 7° 35' 60.00" N; Longitude: 4° 10' 59.99" E, as shown in Figure 1) in Ayedire LCDA, Osun State of South-Western Nigeria was the location of the study. Osun State is located between latitudes 7.0° and 8.0° N and longitudes 04°.10' and 05°.05' E, and it has a total area of roughly 14,875 km^2. The state experiences annual rainfall ranging from 1125 mm in the north to 1475 mm in the south. South-Western Nigeria's lowland rain forest zone is home to the vegetation, and Iwo and Osogbo are covered in derived savannah (Abe, 1995). Men's dependence on using medicinal plants for low sperm count may be significant because there aren't many contemporary health facilities in the research area, thus, information on herbs traditionally used to treat males with low sperm counts was the main focus of study. On June 11, 2022, the plants recorded for the treatment of low sperm count were chosen from the ancestral document of medicinal plants used for the treatment of male infertility, under the care of Mr. Moslem Abeeb, the Director of Ifa Tradomedical Centre, Oluponna, Osun state, Nigeria. Low sperm count was literally referred to in the book as "watery sperm". All specified plant species have been verified and the scientific names have been updated with relevant research publications. To document the phytochemical components of the therapeutic plants mentioned, literatures were also used.

RESULTS AND DISCUSSION

The study area

Varying knowledge of medicinal plants used in the treatment of low sperm count in Oluponna clearly shows that it's a "different stroke for different folks" endogenous knowledge of medicinal plants. Usually, traditional healers are specialist in different approaches in the preparation of medicinal concoctions due to their knowledge in traditional usage coupled with the efficacy of these plants. A total of thirteen medicinal plants, (Table 1) used by the people of Oluponna area of the Ayedire local government of Osun state for the treatment of low sperm count, documented and identified in the study area.

Ethnomedicinal effect of plants recorded in the document

The identified plant species belongs to ten families and twelve genera. In this enumeration (Table 1), plants were arranged in alphabetical order with plant families, botanical names, plant part used, formulation and application as well as previous literature documentation and reported bioactive compounds. The most cited family in the document was Apocynaceae, which had three species, *Alstonia boonei*, *Landolphia dulcis*, and *Rauwolfia vomitoria*, two members of the family Armyllidaceae, *A. sativum* and *A. ascalonicum*, and one member of each of the following families: Amplidaceae, Cassalpiniaceae, Euphobiaceae, Lamiaceae and Meliacea Each plant identified in the document examined has been used by the respondent and is said to be effective based on the knowledge passed on to him and the feedbacks gathered over decades of extensive recommendation of these plants. This traditional healer's plant recipes range from single plant to multi-plant preparations.

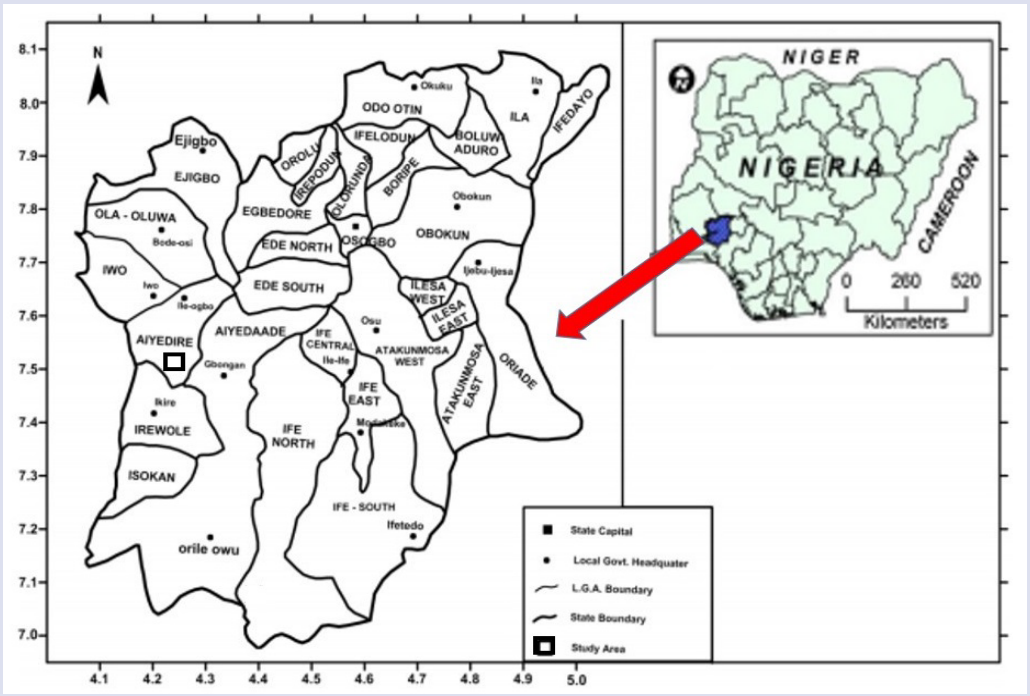

Figure 1: Map showing the study areas in South-Western Nigeria.

Table 1: Medicinal herbs mentioned in the ethnobotanical survey for treatment of low sperm counts.

	Family	Species	Part used	Formulation; Application	Cited for male infertility	Bioactive compounds	References
1.	Amaryllidaceae	*Allium sativum*	Whole plant	-	Enhances male sexual performance and is useful for the restoration of testicular function	Ajoenes (E-ajoene, Z-ajoene), thiosulfinates (allicin), vinyldithiins (2-vinyl-(4H)-1,3-dithiin, 3-vinyl-(4H)-1,2-dithiin), sulfides (diallyl disulfide (DADS), diallyl trisulfide (DATS), S-propyl-cysteine-sulfoxide (PCSO), allicin, S-methyl cysteine-sulfoxide (MCSO).	26-28, 53
2.	Amaryllidaceae	*Allium ascalonicum*	Whole plant	-	-	furost-5(6)-en-3beta,22alpha-diol 1beta-O-beta-D-galactopyranosyl 26-O-[alpha-L-rhamnopyranosyl-(1-->2)-O-beta-D-glucopyranoside], furost-5(6),20(22)-dien-3beta-ol 1beta-O-beta-D-galactopyranosyl 26-O-[alpha-L-rhamnopyranosyl-(1-->2)-O-beta-D-glucopyranoside], 3,24-acetonideclethric acid, ursolic acid, randiasaponin IV, ilekudinoside W, (25S)-1β,3β,24β- trihydroxyspirost-5-en 1-O-α-L-rhamnopyranosyl-(1→2)- α-L-arabinopyranoside.	29, 30
3.	Amplidaceae	*Cissus popunea*	Root	Soaking in water for 24 h.	Stem bark, over a 72-day period in man had no fertility enhancement effects, while oral administration its aqueous extract improves spermatogenesis in male wistar rats	Bergenin, physcion, chrysophanol.	31, 32, 55, 56
4.	Apocynaceae	*Landolphia dulcis*	Leaf	Juice of lime with equal amount of leaf juice.		(2S,4R,5S,6R,7R)-2-Hydroxy-1(10)-aromadendren-14-oic acid, 2,14-lactone, (2S,4R,5S,6R,7R,9S)-2,9-Dihydroxy-1(10)-aromadendren-14-oic acid 2,14-lactone, (2S,4R,5S,6R,7R,11S)-2,12-Dihydroxy-1(10)-aromadendren-14-oic acid 2,14-lactone, (4R,5S,6R,7R,11S)-12-Hydroxy-1(10)-aromadendren-2-one, (4R,5S,6R,7R,11S)-2-Oxo-1(10)-aromadendren-12-oic acid, (4R,5S,6R,7R,11S)-12-Hydroxy-1(10)-aromadendren-9-one, Methyl (4R,5S,6R,7R,11S)-2,9-dioxo-1(10)-aromadendren-12-oat, (4R,5S,6R,7R,11S)-12-Hydroxy-1(10)-aromadendren-14-al, (1R,6R,7R,10R,11S)-12-Hydroxy-4(5)-aromadendren-3-one, (1R,6R,7S,10R)-10-Hydroxy-4(5)-cadinen-3-one, (1S,6R,7S,10R)-10-Hydroxy-4(5)-muurolen-3-one.	33
5.	Apocynaceae	*Rauvolfia vomitoria*	Root	-	In albino rats, the back increases sperm motility, count, and transit.	Stigmasterol, β-sitosterol, Rauvine A, Rauvine B.	28, 34, 57, 58
6.	Apocynaceae	*Alstonia boonei*	Stem back	Powder of the bark and *P. guineense*	In addition to reversible antifertility effects in male rats, stem back may have harmful potentials on reproductive function without the involvement of plasma testosterone.	Rutin, Quercetin robinobioside, Kaempferol-3-O-rutinoside, Kaempferol-3-O-robinobioside, Kaempferol-3-O-[α-L-rhamnopyranosyl (1→4) β-D-glucopyranoside, Quercetin-3-O-[α-L-rhamnopyranosyl(1→4) β-Dglucopyranoside]., Quercetin-3-O-[α-L-rhamnopyranosyl(1→2) β-D glucopyranoside], Quercetin-3-O-[α-Lrhamnopyranosyl(1→2) β-D-galactopyranoside].	35, 36, 64
7.	Ceasalpiniaceae/ Fabaceae	*Ceasalpinia bonducella*	Root	Root soak in 7-up drink	The root increased rat male sexual behaviour and may have aphrodisiac properties.	Quercetin-3-methyl ether, kaempferol, kaempferol-3-O-α-L-rhamnopyranosyl-1→2)-β-D-xylopyranoside, hematoxylol, stereochenol A, 6′-O-acetylloganic acid, 4′-O-acetylloganic acid, 2-O-β-d-glucosyloxy-4-methoxybenzenepropanoic acid.	37-39

8.	Euphorbiaceae	*Jathropha curcas*	Fruit	Dried fruit burn together with local (black) soap and potash. The powder will be taken with hot pap.	None	Campesterol, stigmasterol, b-sitosterol, phytol, phytol, hexacosan-1-ol, octacosan-1-ol, triacontan-1-ol.	40
9.	Lamiaceae	*Clerodendron polycephalum*	Leaf	Leaf juice	None	None	
10.	Meliaceae	*Khaya ivorensis*	Stem back	The chars of the back mixed with black soap	Male infertility may result from the severe effects on the testicles and spermatogenic activity that derive from extract of stem bark.	14,15-didehydroruageanin A, 3-O-methyl- butyrylseneganolide A, seneganolide A, 1,3-dideacetylkhivorin, 7-deacetylkhivorin, 3-deacetylkhivorin, 1-deacetylkhivorin, and 3-deacetyl-7-oxokhivorin, 2-hydroxymexicanolide, 6-deoxydestigloylswietenine, 2, 6-dihydroxy-3-mexicanolide.	41-43
11.	Piperaceae	*Piper guineense*	Seed	Powder of *A. boonei* bark and the seed	It stimulated testicular, epididymal, seminal vesicle secretions and a surge in libido and the frequency of male sexual activity	N-pyrrolidyl-2,4-octadecadienamide, N-piperidyl-2,4-octadecadienamide, linalool, 3,5-dimethoxytoluene.	44-47
12.	Polygalaceae	*Securidaca longipendunculata*	Root	-	The root bark extract may be able to boost male animals' fertility, but the dosage and duration of therapy need to be watched carefully.	Caffeic acid, 4,5-dicaffeoyl D-quinic acid, 3,4,5-tricaffeoyl D-quinic acid3, 4-dimethoxy-7-hydroxyxanthone, 3-hydroxy benzoic acid, 3-hydroxy-4-methoxy benzoic acid.	48-50
13.	Portulacaceae	*Talinum triangulare*	Aerial part	Fresh juice	Enhance the motility and viability of spermatozoa, although use should not be prolonged.	Campesterol, sitosterol, stigmasterol, scotenol, 3-(N-acryloil, N-pentadecanoil) propanoic acid, allantoin, malic acid, asparagine, phaeophytin, 13^2-hydroxyphaeophytin, purpurin, 3-(N-acryloil, N-pentadecanoil) propanoic acid, scotenol.	51, 52

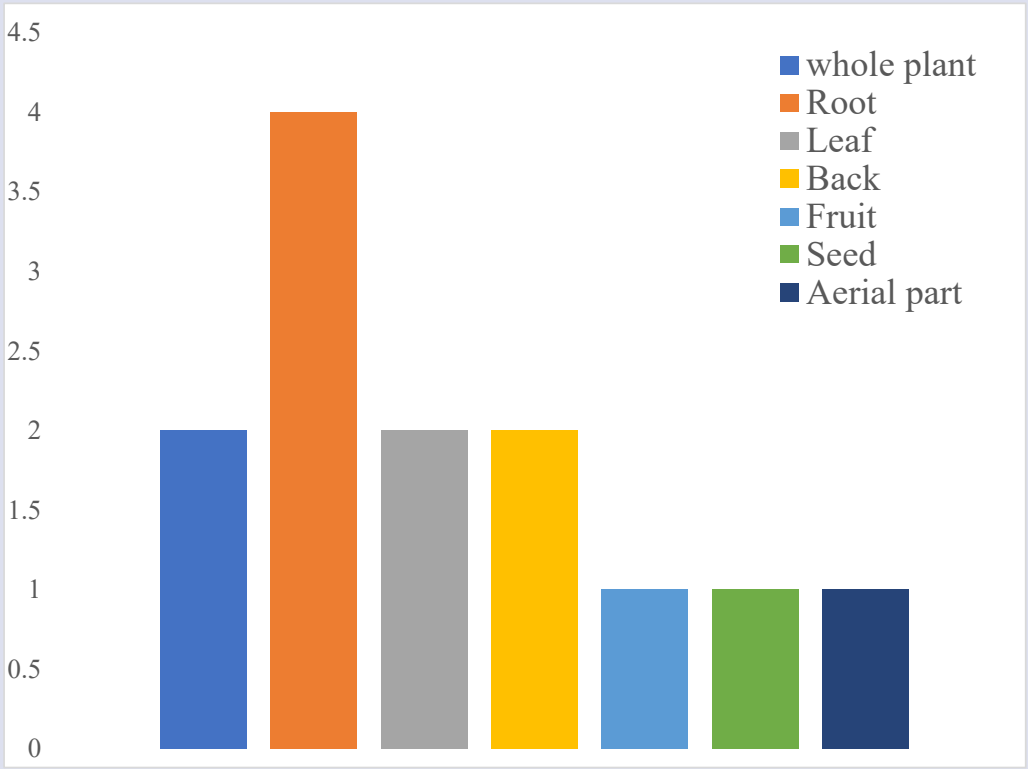

Figure 2: Plant components mentioned as a therapy for low sperm count.

Interestingly, different authors have given credence to the use of some plants reported in the document on their general use for male infertility and other reproductive health issues. For instance, Musavi *et al*. (2018),[53] confirmed the use of *Allium sativum* as a therapeutic plant that can increase fertility due to its antioxidant properties. However, a study on sperm parameters contradicts the use of *A. sativum* for male reproductive health functions. At higher doses, aqueous extract *A. sativum* reduced superoxide dismutase activity and the morphological structure of sperm cells.[54] A study conducted in 2013 backs up the use of *A. ascalonicum* for treating male infertility. After 14 days of treatment with oral doses of 0.5 and 10 g/100g body weight, streptozotocin-induced diabetic mice showed an increase in gonadal index and sperm quality (Ampa *et al*., 2013).

Interestingly, after 64 days of administration, aqueous extract of *Cissus popunea* caused a four-fold increase in sperm count in rats, thereby enhancing spermatogenesis, whereas, *in vivo* study on its crude extracts in human after 72 days administration had no fertility enhancing effects on sperm parameters.[55,56] Furthermore, 200 mg/kg body weight dose of *Rauwolfia vomitoria* was found to increase spermatogenesis in male rats after 21 days administration.[57] Ethanolic extract of *R. vomitoria* improved male sexual behavior and reproduction in rats, thus, justifying the ethnobotanical use of the plant as mentioned in the document.[58] According to Memudu *et al*.,[60] *P. guineense* dried fruits increase testicular hormone secretion, which supports its ethnobotanical use in Nigeria's south western region. *Securidaca longipenduculata* has been reported in the literature as one of the plants used to improve sexual performance and virility and it was discovered to urpsurge testicular parameters in buck rabbits.[61,62] At varying dosages, a crude extract of *Talinum triangulare* was found to have a reversible antifertility effect after a longer period of use.[63]

Raji *et al*. (2005)[64] reported a reversible antifertility effect of *Alstonia boonei* methanolic extract, justifying its ethnobotanical use among traditional healers. Previous research confirms the *Alstonia* genus efficacy on sperm parameters.[65] Some of the plant species described in this study have never been reported to have any effect on male fertility in the literature.These are *Landolphia dulcis*, *Ceasalphinia bonducella* bark, *Jatropha curcas* fruits, *Clerodendron polycephalum* leaves and *Khava ivorensis* stem bark (Figure 2). Meanwhile, Meerwal and Jain (2016)[66] as well as Tripathy *et al*. (2018)[67] reported that ethanolic extracts of *Ceasalphinia bonducella* seed, at higher dose displayed antifertility effects in male wistar rats, thus, could be use as a male contraceptive.

CONCLUSION

Thirteen medicinal plants were found in the ancestral record of local recipes used for management of low sperm count in Oluponna community. This validated the use of botanicals traditionally for treatment of low sperm count. The method of preparation for many of these plants are handed down to the next generation through properly writing documentation. This demonstrates that Oluponna flora contains a variety of medicinal plants used in the treatment of different ailments including low sperm count as well as the knowledge of their application. Since this is the first review on the documentation of an ancestral knowledge and application of medicinal plants as means of passing the knowledge from a generation to another in Oluponna, additional toxicological and pharmacological studies are hereby recommended in order to provide scientific rationale for the long-term knowledge and use of these plants.

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ETHICAL DISCLOSURES

The authors declare that no experiments were performed on humans or animals for this study.

CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

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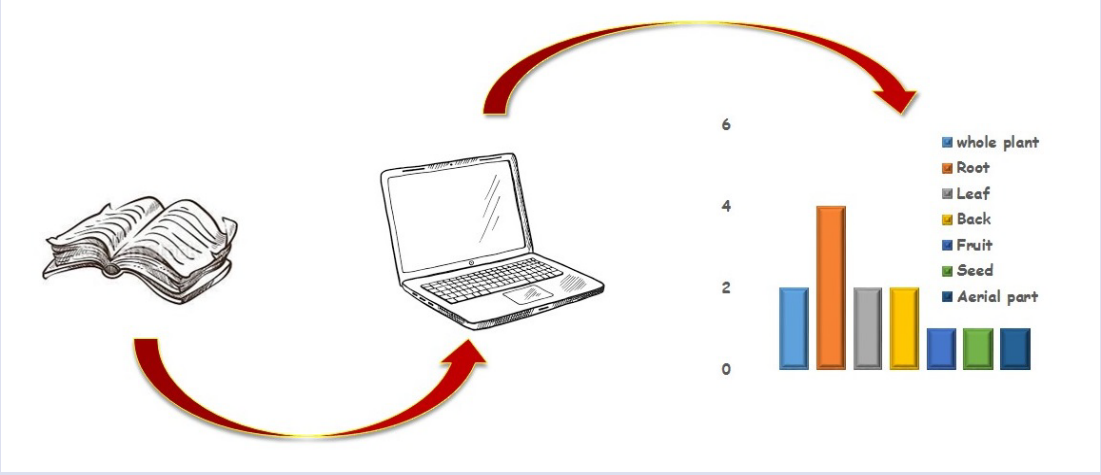
GRAPHICAL ABSTRACT



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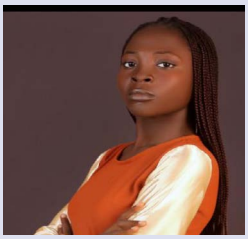

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