

Special Article - Complementary Medicine

Uterine Fibroids Management by a Popular Traditional Practitioner in Bobo-Dioulasso, Burkina Faso

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Abstract

Ethnopharmacological Relevance: Uterine fibroids are the most common benign tumours in women of reproductive age. It represents the most frequent gynaecological pathology among outpatients from the Department of Gynaecology in some teaching hospitals in Burkina Faso. Besides conventional treatments, there is a traditional medicine that is widely used by African populations. This study aims at investigating uterine fibroids management in traditional medicine.

Materials and Methods: Structured interviews were administered to the traditional healer and her patients. Ultrasound examination reports were collected. The rationale for the use of the plants was discussed.

Results: *Trichilia emetica*, *Securidaca longepedunculata*, *Cassia sieberiana* and *Lannea acida* were used to treat uterine fibroids. Decoction of the mixture from these plants was used as an oral drink, vaginal baths and sitz bath. In addition to the plants, abdominal expression to extract masses from the pelvis. The mean size of the uterus is 1694421mm vs. 1663637mm; the mean number of fibroids is 6.67 vs. 8; the mean size of fibroids is 3158.67mm³ vs. 3216mm³ and the mean size of the ovaries 1405mm³ vs. 1774mm³ before and after treatment respectively.

Conclusion: The plants used by the traditional healer are involved in some pathophysiological pathways of uterine fibroids and justify their use. Further studies to investigate ultrasound outcome, anatomopathological examinations of extracted masses are needed.

Keywords: Uterine fibroids; Burkina Faso; Traditional medicine

Introduction

Uterine fibroids or leiomyomas are the most common benign tumours in women of reproductive age. The prevalence of fibroids varies among different studies and countries (4.5%-68.6%) based on the type of investigation, method of diagnosis, and racial/ethnic demographics of the population studied [1]. Recent research from the United States has shown that fibroids are detected by ultrasound in more than 80% of women of African ancestry and nearly 70% of white women by the age of 50 [2]. In Burkina Faso, there are no data available on its prevalence. However, it has been shown that it is the most frequent gynaecological pathology among outpatients from Department of Gynaecology at Yalgado Ouedraogo Teaching Hospital of Ouagadougou [3]. Uterine fibroids (47.3%) were also found to be the dominant cause of gynaecological indications of hysterectomy [4].

Many are discovered incidentally on clinical examination or imaging in asymptomatic women [5]. Though most women with fibroids are asymptomatic, approximately 30% of them will present with severe symptoms, which can include abnormal uterine bleeding, anaemia, pelvic pain and pressure, back pain, Pollakiuria, constipation, or infertility, and will require intervention. Furthermore, fibroids have been associated with poor obstetrical outcomes [6].

Treatment options improve fibroid-associated symptomatology

by reducing the size of the fibroids, controlling fibroid-related abnormal uterine bleeding, or definitively curing the fibroids. Available treatments include medical therapies, interventional radiology, and surgical procedures. Despite the advancement of medical and uterine-preserving treatment options in the past decade, hysterectomy remains the most commonly offered and chosen treatment by women with symptomatic fibroids [6,7]. In Africa, in addition to conventional treatments, traditional medicine, which is used by 80% of the populations [8] offers phyto-treatments for the management of leiomyomas [9-13]. These plants play important role as alternative medicine due to their low cost, perception of their minimal side effects, availability and knowledge about their use in the treatment of diseases. Many African plants have been shown to have Anti-Uterine Fibroid effects in animal models [11,13-17].

Some traditional healers are specialized in the management of gynaecological affections of women. In Bobo-Dioulasso, a very popular traditional healer is known to treat uterine fibroids and women fertility problems. She is receiving patients from all over West Africa. We aimed at studying the treatment uterine fibroids and its outcomes by a popular traditional healer in Bobo-Dioulasso.

Materials and Methods

Study area

The study was carried out in Bobo-Dioulasso. Bobo-Dioulasso is

the second largest city in Burkina Faso with an estimated population of 860,426 inhabitants in 2019 (Institut National de la Statistique et de la Démographie (INSD), [18]). It is located in the western part of the country (11°10'7.31"N, 4°17'52.24"W).

Study type and study period

It was a cross-sectional study with a descriptive and analytical aims that took place from November 25 to December 24, 2016 in Bobo-Dioulasso.

Study population

The study investigated two populations:

- Patients coming for a consultation with the traditional healer during the period of our study with uterine fibroids established by an ultrasound examination.
- The traditional healer knowledge and practices.

Sample and sampling

A sample of ten (10) women responding to inclusion criteria and agreeing to participate were enrolled.

Sampling methods: systematic, consisting of the patients around at the traditional healer place on the day of the survey; consenting to participate and holding pre- and post-treatment's ultrasound examinations.

The selection of the traditional healer is reasoned because of her notoriety in Bobo-Dioulasso and beyond Burkina Faso. She received a national decoration and was subject to several media reports.

Collection of data

Informal and formal conversations, discussions, and semi-structured interviews as well as field visits were conducted [19]. A series of individual interviews were carried out to gather information regarding the name, age, sex, level of education, occupation, symptomatology, history of the disease, and treatment. Moreover, respondents were asked about local names of medicinal plants used, part used, mode of preparation.

The ultrasound examinations were used to follow up the evolution of uterine fibroids before and after treatment.

Results

The traditional healer

The traditional healer was 57 years old at the time of the survey. She said she inherited and learnt from her dad. She has 26 years of experience in the practice of TM.

The patients

Most of them come from Bobo-Dioulasso and its neighbourhoods. Some are coming from sub-Saharan African countries including Togo, Gabon, Senegal, Mali, United-States. She has received and treated two white ladies from France and Canada.

Some patients are referred by other traditional healers of Bobo-Dioulasso, by the recommendation of other people/patients.

About 10 women come to the clinic every day for uterine fibroids including those coming for their follow up.

In this study, 6 patients were enrolled. They were at the traditional

Table 1: Plants used by the traditional healers to treat uterine fibroids.

Botanic name	Family	Name in mooré
<i>Trichilia emetica</i> Vahl	Meliaceae	Kikiristaaga
<i>Securidaca longepedunculata</i> Fers	Polygalaceae	Pelga
<i>Cassia sieberiana</i> DC	Caesalpinoideae	Kombrisaaka
<i>Lannea acida</i> A. Rich	Anacardiaceae	Samtuliga

Table 2: Ultrasound outcomes before and after the treatment.

	Mean size of the Uterus (mm ³)	Mean number of fibroids	Mean size of fibroids (mm ³)	Mean size of the ovaries (mm ³)
Before treatment	1694421	6.67	3158.7	1405
After treatment	1663637	8	3216	1774
Difference	30784	-1.33	-57.33	369

healers on the day of the questionnaire administration with pre- and post-treatment ultrasound examinations available. They were administered a semi-structured questionnaire and the ultrasound results before and after treatment was collected.

The treatment

Aims of the treatment: According to the traditional healer, the treatment aims at resorption of the pelvic mass and regression of the pain.

Plants used: Four plants are used (Table 1).

Stem bark and roots of the four plants are used together in the below described preparation.

Preparation technics: All the plant materials are air dried under the sun as shown in Figure 1.

- *Trichilia emetica* Vahl and *Cassia sieberiana* DC are grounded to obtain fine powder;
- *Trichilia emetica* Vahl, *Securidaca longepedunculata* Fers, *Cassia sieberiana* DC and, *Lannea acida* A. Rich are boiled together in an unspecified quantity for about 10 hours in 20 litres cooking pot.

Administration mode:

- Half a litre of the decoction is to be administered orally for 2 months;
- Powder of *Trichilia emetica* Vahl is mixed in cold water. The mixture is to be drunk 3 times a day and to be used as a vaginal bath and sitz bath;
- Powder of *Cassia sieberiana* is mixed in cold water. The mixture is to be drunk 3 times a day.

Other treatments

Other treatments include vaginal cleaning with gloved hands, raise the posed organs into uterine cavity tumours and abdominal expression for vaginal delivery of tumours. On Figure 2, the traditional healer is expressing the abdominal and pelvic cavities for delivering some masses showed on Figure 3. Figure 3 is showing organic masses extract from a women womb via her vagina by the traditional healer.

One patient had submucosal fibroids that was not seen after the treatment ultrasound examination (Table 2).



Figure 1: Plants used in the fibroid treatment being dried under the sun in the "hospital".



Figure 3: Masses extracted from the pelvic-abdominal cavity through the vagina.



Figure 2: Traditional healers expressing pelvic and abdominal cavities to extract masses through the vagina.

One patient had ovary cyst that was not seen after the treatment ultrasound examination.

Discussion

This pilot study describes uterine fibroid treatments and outcomes at a popular traditional healer of Bobo-Dioulasso. The treatment is made of plants.

The main limitation of this study is the limited population size. The non-intervention design does not allow confident comparability across ultrasound examinations as there were performed by different operators with different apparatus. However, this pilot study gives useful insights into uterine fibroids management and potential outcomes.

Sex steroid hormones, deregulation of cell signaling pathways, miRNA expression, and cytogenetic abnormalities, oxidative stress may all implicate in fibroid aetiology. Several herbal medicines have been used as anti-inflammation and antitumor agents. All of them have a common capability to inhibit the expression of pro-

inflammatory cytokines, proliferative genes, and pro-angiogenic genes, which are useful in the management of uterine fibroids [20].

Trichilia emetica Vahl

Antioxidant activities: Numerous studies demonstrated antioxidant proprieties of flavonoids extracts from *Trichilia emetica*. The extracts submitted to alkaline hydrolysis showed high antioxidant properties in two in vitro assays: autoxidation of Methyl Linoleate (MeLo) and ascorbate/Fe²⁺-mediated lipid peroxidation in rats microsomes [21] and other results obtained revealed that methanol extract has presented significant IC₅₀=5.94µg/mL radical scavenging activity [22].

Anti-inflammatory activities: The anti-inflammatory activities of *Trichilia emetica* was evaluated by some studies.

Two solvent extracts (ethanol and water) were screened for anti-inflammatory activity. At a concentration of 5 mg/ml, the percentage inhibition of prostaglandin synthesis was 22% and 89% for ethanol and aqueous leaf extracts. The plant extracts showed higher inhibitory activity than indomethacin (0.5mg) [23]. Sanogo et al. studied the anti-inflammatory activities of aqueous extracts of leaves, bark and roots of these plants. The extracts possess significant anti-nociceptive and anti-inflammatory activities at the dose of 25mL/kg administered orally in mice compared to control group ($P < 0.05$, test *t*-Student) [24].

Antitumor and anticancer activities: Limonoids extracted from *Trichilia emetica* showed selective inhibitory activity toward DNA repair-deficient yeast mutants [25].

Heat shock protein 90 (Hsp90), an evolutionarily conserved molecular chaperone, is involved in the folding, stabilization, activation and assembly of a wide range of "client" proteins, thus playing a central role in many cellular processes [26]. This protein is involved in oestrogen pathways in uterine leiomyoma cells [27,28]. Dal Piaz et al. [29] indicated this compound as a type of client selective Hsp90 inhibitor, directly binding to the middle domain of the protein and possibly preventing its interaction with the activator of Hsp90 ATPase 1 [29].

***Securidaca longepedunculata* Fers**

Antioxidant activities: Data on antioxidant activities of *Securidaca longepedunculata* are controversial, some supporting its antioxidant properties while others showing oxidative stress induction.

The IC₅₀ of the root barks of *Securidaca longepedunculata* value reached 5.5 µg/ml, revealing that they have a very high antioxidant activity [30]. *Securidaca longepedunculata* represents natural sources of phenolic antioxidant compounds [31]. The results from Abonyi et al. suggest a moderate antioxidant activity [32]. While Ajoboye et al. demonstrated that aqueous extract of *Securidaca longepedunculata* root, induce redox imbalance in male rat liver and kidneys. They found that there was also significant decrease ($p < 0.05$) in the activities of superoxide dismutase, catalase, glutathione peroxidase and glutathione reductase in the liver and kidney. Liver and kidney levels of GSH, vitamins C and E were also significantly reduced ($p < 0.05$). Serum malondialdehyde and lipid hydroperoxides increased significantly ($p < 0.05$) in all the extract-treated groups [33]. Anyebe et al. reached to the same results in mice. Methanol leaf extract of *Securidaca longepedunculata* increases lipid peroxidation with increase in dosage [34].

Anti-inflammatory activities: The results from an experimental animal study indicate that *Securidaca longepedunculata* root-bark aqueous extract possesses analgesic and anti-inflammatory properties. The magnitude of activity obtained at the two dose levels (5 and 10 mg/Kg) used indicates high potency of anti-inflammatory effect [35]. Both the leaf and stem methanol extracts exhibited anti-inflammatory activity greater than 70% of all doses tested [36].

Antitumor and anticancer activities: Some studies have shown anti-tumoral activities of extracts from *Securidaca longepedunculata*. The extracts significantly ($p < 0.05$) inhibited the proliferation of U87 and U231 brain tumor cell lines with the respective IC₅₀ values ranging between 8 and 20 µg/ml for *Securidaca longepedunculata* [37]. In addition, CHCl₃ extracts of the roots of *Securidaca longepedunculata* displayed the potent preferential cytotoxicity with PC50 of 22.8 and 17.4 µM, respectively. They triggered apoptosis-like PANC-1 cell death in NDM with a glucose-sensitive mode [38]. Brine shrimp toxicity assay showed a LC₅₀ of 25.1 µg/mL and the *Allium cepa* assay revealed that 100 mg/mL extract caused a reduction in Mitotic Index (MI) which was comparable to that of the standard drug, methotrexate. *Securidaca longepedunculata* has potential as a cytotoxic agent [39].

***Cassia sieberiana* DC**

Antioxidant activities: Extracts from *Cassia sieberiana* roots bark extract has been shown to exhibit antioxidant activities. The root bark extract of *Cassia sieberiana* was found to possess significant ferric reducing antioxidant power and can scavenge hydroxyl radicals [40]. Same results with the crude extract from the roots were found by Kpegba et al. They realized a set of complementary assays, i.e., radical scavenging, ferric reduction, and inhibition of lipid peroxidation, were conducted to evaluate the antioxidant activity of the crude extract, which showed strong antioxidant properties [41]. Leaves [42] and bark [43] also have an appreciable antioxidant power.

Anti-inflammatory activities: *Cassia sieberiana* possesses anti-

inflammatory plus analgesic properties. *Cassia sieberiana* leaves modulate LPS-induced inflammatory response in THP-1 cells and inhibit eicosanoid-metabolizing enzymes [44]. The aqueous root extract of *Cassia sieberiana* possessed both analgesic and anti-inflammatory activities [45]. It was demonstrated that the anti-inflammatory activity of extracts of root bark of *C. sieberiana* may be attributable to their immunomodulatory effects via suppression of pro-inflammatory cytokines, TNF- α , IL-1 α and IL-6; and elevation of the anti-inflammatory cytokine, IL-10 levels, in serum [46].

Antitumor and anticancer activities: No data on antitumor and antiproliferative effects of *Cassia sieberiana* was retrieved in the literature.

***Lannea acida* A. Rich**

Antioxidant activities: The stem and roots of *Lannea acida* contain flavonoids that were shown to have important radical scavenging activity [47]. Ouattara et al. investigated the antioxidant activities of ethanol bark extracts of *Lannea acida* using the 2,2'-diphenyl-1-picrylhydrazyl (DPPH) free radical scavenging assay with gallic acid and quercetin as positive controls. The extract exhibited IC₅₀ value of 345.7 µg/mL, while the controls, gallic acid and quercetin exhibited much lower IC₅₀ values of 0.6 µg/mL and 0.9 µg/mL, respectively [48].

Anti-inflammatory activities: A study by Owusu et al. evaluated anti-inflammatory and analgesic effects of *Lannea acida* in rodents. Aqueous extract (30-300 mg/kg) of *Lannea acida* stem bark significantly reduced prostaglandin E₂-induced paw oedema in both prophylactic and curative protocols. The extract also significantly inhibited acetic acid-induced abdominal writhing movement in Imprint Control Region (ICR) mice.

Antitumor and anticancer activities: Bruna and his collaborators investigated the dichloromethane extract *Lannea acida* activities against Multiple Myeloma Cancer Stem Cells, of the plant's root bark inhibited the cell growth at 20 µg/mL (<30% of cell growth). A bioassay-guided fractionation was performed to isolate and identify active molecules that inhibits the cell proliferation, using analytical techniques such as High-Performance Liquid Chromatography, Mass Spectrometry, Nuclear Magnetic Resonance, Infrared, Ultraviolet-visible and Circular Dichroism spectroscopies, specific rotation and MTT-proliferation assay. Using these techniques, four new and active molecules with similar structures were isolated. They have comparable inhibition concentrations (IC₅₀), surrounding 10-15 µM, in MM-CSCs, which are drug-resistant cells, responsible for some cancer relapses [49].

Oestrogenic activities: Oumarou et al. evaluated the oestrogenic activities of bark ethanolic extracts of *Lannea acida* [50]. The basic principle of this assay is to compare the MCF-7 cells yield following treatment with tested substances with those obtained after oestradiol treatment. In this study, the *Lannea acida* ethanol extract induced a significant increase of MCF-7 cells proliferation at concentrations of 10, 100, and 200 µg/mL as compared to DMSO control. The MCF-7 cell proliferation is known as a hallmark of estrogenicity (Oumarou et al., 2017). This oestrogenic activity is not in favour of anti-uterus fibroids activities. Oestrogen has been shown to stimulate proliferation in a dose- and time-dependent manner in uterine fibroid cell lines [27,51]. Oestrogen (17 β -oestradiol) binds to the nuclear oestrogen receptor

(ER)- α to modulate the expression of protooncogenes, cytokines, and growth factors [20,52].

Interestingly, a recent study demonstrated that *Lannea acida* possesses uterotonic effects mediated through oxytocin receptors with mobilization of extracellular calcium. The authors found that *Lannea acida* induced uterine contraction in a concentration-dependent manner with the methanol extract (1.506 ± 0.032 gf) being the most effective. Administration of atosiban ($2\mu\text{mol/L}$) and atropine ($1\mu\text{mol/L}$) reduced the contractile effect of *Lannea acida*. Complete inhibition was observed with nifedipine, 2-APB, and calcium-free medium containing EGTA [53].

The manipulation in the vagina orifice practiced by traditional healers, without even inducing bleeding is difficultly explainable. However, these manipulations could be dangerous; it could lead to haemorrhage or infections due to lack aseptic measures.

Conclusion

The traditional management of uterine fibroids by the traditional healer is mainly consisted of four plants: *Trichilia emetica*, *Securidaca longepedunculata*, *Cassia sieberiana* and *Lannea acida*. All these plants are active against some pathophysiological components of uterine fibroids and might justify their use. Studies to investigate the clinical outcomes, the anatomopathological examination of the extracted masses and anti-uterine fibroids in animal models are needed.

Declaration

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References

- Stewart EA, Cookson CL, Gandolfo RA, Schulze-Rath R. Epidemiology of uterine fibroids: a systematic review. *BJOG*. 2017; 124: 1501-1512.
- Baird DD, Dunson DB, Hill MC, Cousins D, Schectman JM. High cumulative incidence of uterine leiomyoma in black and white women: ultrasound evidence. *Am J Obstet Gynecol*. 2003; 188: 100-107.
- Alexis SY, Issa O, Sibraogo K, Boubakar T. Pathologies and Affections Diagnosed in Outpatient Department of Gynecology at Yalgado Ouedraogo Teaching Hospital of Ouagadougou, Burkina Faso. *International Journal of Current Innovations in Advanced Research*. 2018; 1: 156-162.
- Ouattara A, Gueswendé KFX, Rodrigue SS, Danielle MF, Issa O, Boubakar T, et al. Indications and Prognosis of the Hysterectomy Operation in the Obstetrics and Gynecology Department at the University Teaching Hospital of Ouagadougou (UTH-YO), Burkina Faso. *Open Journal of Obstetrics and Gynecology*. 2017; 7: 1239-1246.
- De La Cruz MSD, Buchanan EM. Uterine Fibroids: Diagnosis and Treatment. *Am Fam Physician*. 2017; 95: 100-107.
- Giuliani E, As-Sanie S, Marsh EE. Epidemiology and management of uterine fibroids. *Int J Gynaecol Obstet*. 2020; 149: 3-9.
- Stewart EA, Laughlin-Tommaso SK, Catherino WH, Lalitkumar S, Gupta D, Vollenhoven B. Uterine fibroids. *Nat Rev Dis Primers*. 2016; 2: 16043.
- Bodeker G, Ong C-K, Grundy C, Burford G, Shein K, Medicine WHOP. WHO Centre for Health Development. WHO global atlas of traditional, complementary and alternative medicine. 2005.
- Ciebiera M, Ali M, Prince L, Jackson-Bey T, Atabiekov I, Zgliczyński S, et al. The Evolving Role of Natural Compounds in the Medical Treatment of Uterine Fibroids. *Journal of Clinical Medicine*. 2020; 9: 1479.
- Fasola TR. An ethnobotanical survey of plants used in the management and treatment of female reproductive health problems in Ibadan, Southwestern Nigeria. *Journal of Biology, Agriculture and Healthcare*. 2015; 5: 7-11.
- N'Guessan K, Kouassi Konan E, Tiébré MS. Plantes utilisées dans le traitement des troubles gynéco-obstétriques par les peuples Abbey et Krobou d'Agboville (Côte-d'Ivoire). *Phytothérapie*. 2009; 7: 262.
- Olapade E, Olapade Clement, Olapade Christiana, Olapade J. Recent Successes in the Use of Natural Herbal Remedies for the Treatment of Intra-uterine Fibroids without Surgery. *HortScience*. 2004; 39: 860E-861.
- Tsobou R, Mapongmetsem PM, Van Damme P. Medicinal Plants Used for Treating Reproductive Health Care Problems in Cameroon, Central Africa. *Econ Bot*. 2016; 70: 145-159.
- Diallo F. Etude phytochimique et activité antiradicalaire de trois plantes médicinales utilisées dans la prise en charge du fibrome utérin au Mali (Thesis). USTTB. 2020.
- Obochi GO, Malu SP, Obi-abang M, Alozie Y, Iyam MA. Effect of Garlic Extracts on Monosodium Glutamate (MSG) Induced Fibroid in Wistar Rats. *Pakistan Journal of Nutrition*. 2019; 8: 970-976.
- Roshdy E, Rajaratnam V, Maitra S, Sabry M, Allah ASA, Al-Hendy A. Treatment of symptomatic uterine fibroids with green tea extract: a pilot randomized controlled clinical study. *Int J Womens Health*. 2013; 5: 477-486.
- Zakaria N, Mohd KS, Saeed MAA, Hassan LEA, Shafaei A, Al-Suede FSR, et al. Anti-Uterine Fibroid Effect of Standardized Labisia Pumila Var. Alata Extracts *In Vitro* and in Human Uterine Fibroid Cancer Xenograft Model. *Asian Pac J Cancer Prev*. 2020; 21: 943-951.
- Institut National de la Statistique et de la Démographie (INSD). *Annuaire statistique 2019*. Ouagadougou, Burkina Faso. 2020.
- Cotton CM, Wilkie P. *Ethnobotany: principles and applications*. John Wiley & Sons Chichester. 1996.
- Li Z-L, Huang T-Y, Ho Y, Shih Y-J, Chen Y-R, Tang H-Y, et al. Herbal Medicine in Uterine Fibroid. *Fibroids*. 2020.
- Germanò MP, D'Angelo V, Biasini T, Sanogo R, De Pasquale R, Catania S. Evaluation of the antioxidant properties and bioavailability of free and bound phenolic acids from *Trichilia emetica* Vahl. *Journal of Ethnopharmacology*. 2006; 105: 368-373.
- Perumal A, Naidu Krishna SB, Sershen Pillay K, Govender P. Phytochemical composition and biological investigation of *Trichilia emetica* Vahl. seed extracts. 2020.
- McGaw LJ, Jäger AK, Staden J van. Prostaglandin Synthesis Inhibitory Activity in Zulu, Xhosa and Sotho Medicinal Plants. *Phytotherapy Research*. 1997; 11: 113-117.
- Sanogo R, Diallo D, Maiga A, Tommasi ND, Pasquale RD. Analgesic and anti-inflammatory activities of the aqueous extracts of *Maytenus senegalensis*, *Stereospermum kunthianum* and *Trichilia emetica* used in the treatment of dysmenorrhoea in Mali. *Planta Med*. 2006; 72: 258.
- Gunatillaka AA, Bolzani V da S, Dagne E, Hofmann GA, Johnson RK, McCabe FL, et al. Limonoids showing selective toxicity to DNA repair-deficient yeast and other constituents of *Trichilia emetica*. *J Nat Prod*. 1998; 61: 179-184.
- Mahalingam D, Swords R, Carew JS, Nawrocki ST, Bhalla K, Giles FJ. Targeting HSP90 for cancer therapy. *Br J Cancer*. 2019; 100: 1523-1529.
- Borahay MA, Al-Hendy A, Kilic GS, Boehning D. Signaling Pathways in Leiomyoma: Understanding Pathobiology and Implications for Therapy. *Mol Med*. 2015; 21: 242-256.

28. Borahay MA, Asoglu MR, Mas A, Adam S, Kilic GS, Al-Hendy A. Estrogen Receptors and Signaling in Fibroids: Role in Pathobiology and Therapeutic Implications. *Reprod Sci.* 2017; 24: 1235-1244.
29. Dal Piaz F, Malafronte N, Romano A, Gallotta D, Belisario MA, Bifulco G, et al. Structural characterization of tetranortriterpenes from *Pseudocedrela kotschy* and *Trichilia emetica* and study of their activity towards the chaperone Hsp90. *Phytochemistry.* 2012; 75: 78-89.
30. Muanda FN, Dicko A, Soulimani R. Assessment of polyphenolic compounds, *in vitro* antioxidant and anti-inflammation properties of *Securidaca longepedunculata* root barks. *CR Biol.* 2010; 333: 663-669.
31. Nitiema LW, Sombié PAED, Koala M, Fiore AD. Phytochemical Composition and Antioxidant Activity of *Balanites aegyptiaca*, *Securidaca longepedunculata* and *Acacia gourmaensis* Used against Seed-borne Fungi in Burkina Faso. *Current Journal of Applied Science and Technology.* 2020: 79-87.
32. O, A, PN, U, Arinze Linus E, Uroko R, et al. *In Vitro* Antioxidant Profile of Methanol Leaf Extract of *Securidaca longepedunculata*. *IOSR Journal of Dental and Medical Sciences.* 2014; 13: 75-81.
33. Ajiboye TO, Salau AK, Yakubu MT, Oladiji AT, Akanji MA, Okogun JI. Aqueous extract of *Securidaca longepedunculata* root induce redox imbalance in male rat liver and kidney. *Hum Exp Toxicol.* 2010; 29: 679-688.
34. Anyebe SS, Anyebe SN, Tende YA, Emmanuel NS, Mshelia PP, Abdulrauf RA, et al. Phytochemical Assessment and Oxidative Stress Biomarkers Evaluation in Swiss Albino Mice Treated with Methanol Leaf Extract of *Securidaca longepedunculata* (*Polygalaceae*). *Journal of Applied Life Sciences International.* 2018: 1-7.
35. Okoli C, Akah P, Ezugworie U. Anti-inflammatory activity of extracts of root bark of *Securidaca longepedunculata* Fres (*Polygalaceae*). *African Journal of Traditional, Complementary and Alternative Medicines.* 2006; 3: 54-63.
36. Alafe AO, Elufioye TO, Faborode OS, Moody JO. Anti-Inflammatory and Analgesic Activities of *Securidaca longepedunculata* Fers (*Polygalaceae*) Leaf and Stem Bark Methanolic Extract. *African Journal of Biomedical Research.* 2014; 17: 187-191.
37. Ngulde SI, Sandabe UK, Abounader R, Zhang Y, Hussaini IM. Activities of Some Medicinal Plants on the Proliferation and Invasion of Brain Tumor Cell Lines. *Adv Pharmacol Pharm Sci.* 2020; 2020: 3626879.
38. Dibwe DF, Awale S, Kadota S, Morita H, Tezuka Y. Hepta-oxygenated xanthenes as anti-austerity agents from *Securidaca longepedunculata*. *Bioorg Med Chem.* 2013; 21: 7663-7668.
39. Lawal RA, Lawal SK, Odesanmi OS, Isiaq O, Adefisan IO, Badmus IA, et al. Brine shrimp cytotoxicity and anti-mitotic activity of aqueous root-bark extract of *Securidaca longepedunculata* (*polygalaceae*). 2018.
40. Nartey ET, Ofosuhenne M, Kudzi W, Agbale CM. Antioxidant and gastric cytoprotective prostaglandins properties of *Cassia sieberiana* roots bark extract as an anti-ulcerogenic agent. *BMC Complementary and Alternative Medicine.* 2012; 12: 65.
41. Kpegba K, Agbonon A, Petrovic AG, Amouzou E, Gbeassor M, Proni G, et al. Epiafzelechin from the Root Bark of *Cassia sieberiana*: Detection by DART Mass Spectrometry, Spectroscopic Characterization, and Antioxidant Properties. *J. Nat. Prod.* 2011; 74: 455-459.
42. Madubuiké GK, Onoja SO, Ezeja MI. Antioxidant and Hepatoprotective Activity of Methanolic Extract of *Cassia sieberiana* Leaves in Carbon Tetrachloride-induced Hepatotoxicity in Rats. *Journal of Advances in Medical and Pharmaceutical Sciences.* 2015: 1-9.
43. Evenamede KS, Kpegba K, Simalou O, Boyode P, Agbonon A, Gbeassor M. Comparative antioxidant potential study of different part of *Cassia sieberiana*. *International Journal of Biological and Chemical Sciences.* 2017; 11: 2924-2935.
44. Macedo T, Ferreres F, Pereira DM, Oliveira AP, Gomes NGM, Gil-Izquierdo Á, et al. *Cassia sieberiana* DC leaves modulate LPS-induced inflammatory response in THP-1 cells and inhibit eicosanoid-metabolizing enzymes. *Journal of Ethnopharmacology.* 2021; 269: 113746.
45. Sy GY, Fall AD, Diatta W, Gueye M, Badji K, Bassegrave E, et al. Analgesic and anti-inflammatory activity of aqueous root extract of *Cassia sieberiana* D.C. (*Caesalpinaceae*). *AJPP.* 2009; 3: 651-653.
46. Donkor K, Woode E, Okine LK. Immunoregulatory activity of root bark of *Cassia sieberiana* D.C. in a modified adjuvant-induced arthritis in rat. *JMPR.* 2017; 11: 613-620.
47. Okoth DA, Chenia HY, Koorbanally NA. Antibacterial and antioxidant activities of flavonoids from *Lannea alata* (Engl.) Engl. (*Anacardiaceae*). *Phytochemistry Letters.* 2013; 6: 476-481.
48. Ouattara L, Koudou J, Zongo C, Barro N, Savadogo A, Bassole I, et al. Antioxidant and antibacterial activities of three species of *Lannea* from Burkina Faso. *J Appl Sci.* 2011; 11: 157-162.
49. Bruna L. Etude phytochimique de *Lannea acida* et son activité antiproliférative sur les cellules souches cancéreuses du myélome multiple. University of Geneva. 2017.
50. Oumarou MR, Zingue S, Bakam BY, Ateba SB, Foyet SH, Mbakop FTT, et al. *Lannea acida* A. Rich. (*Anacardiaceae*) Ethanol Extract Exhibits Estrogenic Effects and Prevents Bone Loss in an Ovariectomized Rat Model of Osteoporosis [WWW Document]. Evidence-Based Complementary and Alternative Medicine. 2017.
51. Al-Hendy A, Diamond MP, El-Sohemy A, Halder SK. 1,25-dihydroxyvitamin D3 regulates expression of sex steroid receptors in human uterine fibroid cells. *J Clin Endocrinol Metab.* 2015; 100: E572-582.
52. Curtis SW, Washburn T, Sewall C, Diaugustine R, Lindzey J, Couse JF, et al. Physiological coupling of growth factor and steroid receptor signaling pathways: estrogen receptor knockout mice lack estrogen-like response to epidermal growth factor. *Proc Natl Acad Sci USA.* 1996; 93: 12626-12630.
53. Ngadjui E, Kouam JY, Fozin GRB, Momo ACT, Deeh PBD, Wankeu-Nya M, et al. Uterotonic Effects of Aqueous and Methanolic Extracts of *Lannea acida* in Wistar Rats: An *In Vitro* Study. *Reprod. Sci.* 2021.