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Review Article

Sphenocentrum jollyanum Pierre (Menispermaceae): From traditional medicine to pharmacological activity and chemical constituents

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ABSTRACT

In Yoruba, southwestern Nigeria, *Sphenocentrum jollyanum* Pierre is known as "Akerejupon". *S. jollyanum* is commonly used in traditional medicine to treat a variety of ailments because of its diverse biological activities. However, a thorough examination of the traditional, pharmacological, and phytochemical properties of *S. jollyanum* is yet lacking. Different plant organs are used as aphrodisiacs, treatments for chronic illnesses including coughs and ulcers, and for malaria by traditional medicinal practitioners. The pharmacological activities of this plant include anti-diabetic, antioxidant, hepatoprotective, anti-inflammatory, antimalarial, anti-allergy, antimicrobial, among others. Some of the isolated compounds from this plant are columbin, isocolumbin, fibleucin, atrotosterone A, pinnatasterone, polypodine B, and 20-hydroxyecdysone. In order to explore this plant for further research and to know its potential effect towards pharmaceutics, the present review aims to provide an updated summary of documents sourced from recent publications regarding ethnomedicinal uses, pharmacology, and phytochemistry of *S. jollyanum*.

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1. Introduction

It is apparent that medicinal plants play an admirable and indispensable role in a range of scientific fields, from the food industry to the fragrance and cosmetics industry to various medical and pharmaceutical techniques (Mohammadhosseini et al., 2021). Medicinal plants are essential to human life and hold a prominent place in many scientific fields. Previous investigations show that several useful natural substances, including coumarins, iridoids, alkaloids, and flavonoids, have been identified in plant materials (Mohammadhosseini et al., 2019).

The medicinal herbs are also said to possess a variety of antibacterial, antioxidant, anti-inflammatory, and anticancer effects. In addition, they are regarded as the foundational elements of ethnobotany and traditional folk medicine in numerous nations throughout the world (Frezza et al., 2019).

Scientific literature studies have demonstrated the effectiveness of medicinal herbs, which are believed to be crucial to maintaining health and developing novel treatments (Mahomoodally, 2013). In addition, comprehensive collections of prospective medicinal plants from Africa and beyond have been reported in terms of ethnopharmacology, phytochemistry, and biological activities (Nalawade et al., 2022; Olaoluwa et al., 2022).

In this regard, Mohammadhosseini et al. (2021) reviewed the curative property, the essential oil profiles, and phytochemistry of genus *Aloysia* (Verbenaceae). The suggestion of further research on less studied species and likely evaluation of toxicological effects of the genus were also reported.

In addition, Olaoluwa et al. (2022) gave a comprehensive review regarding biological activities, ethnopharmacology, and phytochemistry of nine

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selected African *Ficus* species with the aim to open new prospects and strategies for further pharmacological research as a remedy for a variety of ailments and for drug development.The chemical profiles of the essential oils (EOs), non-volatile chemicals, ethnobotany, and biological activities of various plants of the genus *Haplophyllum* from the family Rutaceae were also studied in detail (Mohammadhosseini et al., 2021).The Mediterranean region is home to 40 different species of the genus *Ruta* of the Rutaceae family of citrus trees (Nahar et al., 2021).

Sphenocentrum jollyanum Pierre (Menispermaceae) is a perennial plant that grows to a height of 1.5 m and is commonly found in areas with an annual rainfall of 1800 mm, a mean minimum temperature of 20 °C, and a mean maximum temperature of 29 °C. It grows to an average height of about 1.5 m, with few scanty branches (Iwu, 1993; Olorunnisola et al., 2017). The leaves are wedge-shaped about 5-12 cm and smooth on both sides with a small arrow apex (Iwu, 1993; Olorunnisola et al., 2017). The photograph of *Sphenocentrum jollyanum* is shown in Fig. 1a.

a. (Ref: Gnagbe, (2018)) b. (Ref: Odo-ona, Ibadan, Nigeria)

Fig. 1. The photograph of the aerial parts (a) and seeds (b) of *Sphenocentrum jollyanu*.

The fruit of *S. jollyanum* arises as ovoid-ellipsoid, clusters, with a single large oval shaped seed. It is edible, fleshy, and orange or bright yellow when ripe. The seeds of *Sphenocentrum jollyanum* are shown in Fig. 1b. The roots are visibly bright yellow and are characterized by a sour acidic taste which causes things eaten subsequently to taste sweet (Iwu, 1993; Nia et al., 2004; Olorunnisola et al., 2017).

There is presence of solitary flowers on grown-up branches or on stem between the leaves, this plant has unisexual and regular sepals arranged spirally which increases in size towards the center (Ekpono et al., 2018). *Sphenocentrum jollyanum* is a shrub native to West African tropical forest areas and widely distributed throughout Nigeria, Sierra Leone, Ghana, Cameroon and the Ivory Coast (Nia et al., 2004).

This study presents a review of ethnomedicinal uses, pharmacological activities and phytochemistry of *Sphenocentrum jollyanum*. The only review found on this species was reported by Olorunnisola et al. (2017). Recently, the plant has been extensively studied for various pharmacological activities and phytochemistry. There is a need for an updated comprehensive review on this important species which entails the traditional uses, pharmacology, and phytochemistry. As a result, this study intends to summarize the medicinal potentials of *S. jollyanum* components that have been used in the treatment of a wide range of diseases since ancient times, as well as offer future research strategies. Most importantly, this article is critical of previous studies, focussed attention to inconsistencies and suggested further studies.

2. Methodology

The search terms '*Sphenocentrum jollyanum*', 'ethnomedicinal uses', 'pharmacology', 'isolated compounds', 'bioactivity' was used to find the literature for this review paper across several electronic sources, including Google, Google Scholar, PubMed, Medline, Research Gate, Web of Sciences, and Scifinder. These sources were last accessed on September 6, 2022.

Upper time limit for literature was up till 2022. The search terms were used alone or in various combinations to pool as much literatures as possible. The results were carefully reviewed to check whether they met the inclusion criteria. For example, the articles must be presented in English, focused on ethnobotanical surveys

and ethnomedicinal uses of *Sphenocentrum jollyanum*, the biological activities of the plant, pharmacological activity and phytochemistry. Limitations for inclusion are articles that were not presented in English.

3. Uses of *Sphenocentrum jollyanum*

1.1. Reported ethnomedicinal uses of various organs

Some traditional medicine systems have extensive literature and recordings of theoretical concepts and practical skills, while others are passed down orally from generation to generation (Che et al., 2017).

Some traditional cultures have a large ethnobotanical field, using plants as raw materials to treat a variety of diseases in a safe and sustainable manner while maintaining environmental conservation (Modro et al., 2015; Magalhaesa et al., 2022).

The traditional medical practitioners use different plant organs in folkloric medicine. Some traditional medical practitioners and herb sellers in Southwestern Nigeria use the fruit and root of *S. jollyanum* for treatment of gastric ulcer when ground into powder and drunk with pap or water (Akinwumi and Sonibare, 2019). The root decoction is also used traditionally for treatment of malaria. The root is extensively used as aphrodisiac by men. It is extracted with alcohol for few days and the extract is afterward taken to fortify male erection (Burkill, 1995). The extract is drunk as bitters and this effect is known to be long-lasting. The pulverized root when dried is also used as remedy for muscular pains and fever when mixed with some anti-malarial plants. The aerial part is mixed with *Piper guineense* Schumach. & Thonn. (Family Piperaceae) and lime juice for treating coughs, chronic injuries, and fever. Previous literature revealed that the root is employed for its effectiveness in stimulating the central nervous system (CNS), the management of mental and inflammatory disorders, pain and depression (Oke and Hamburger, 2002). In Nigeria, the roots of *S. jollyanum* once chewed stimulate appetite, relieve constipation, and improve food digestion. The morphological organs of the plant also constitute important components for treatment of sickle cell disease. The roots are also used for managing hypertension, irregular menstrual flow, breast tumor, and diabetes mellitus in herbal medicine of Ghana and Cote d Ivoire (Odugbemi, 2006). Traditional medical practitioners in Ivory Coast believe that the root of *S. jollyanum* has unusual stomachic and hemostatic properties, as well as being an emetic for poisoning (Amidu et al., 2008). In Sub-Saharan Africa, *S. jollyanum* is used as an aphrodisiac and to treat sexual dysfunction (Ajao et al., 2019).

1.2. Biological and pharmacological activity

The medicinal value of plants lies in the bioactive phytochemical constituents that produce definite physiological action on the human body (Abiodun et al., 2017). Medicinal plants remain the significant basis of traditional medicine for the populace. About 80% of people worldwide depend mostly on traditional, mainly herbal medicines for their main healthcare needs (Pei, 2001). Traditional use of plants for managing numerous diseases remains an essential part of traditions of majority of the populace. Furthermore, affordability, availability, and accessibility of medicinal plants are important factors that led to the great request and practice. Several medicinal plants possess secondary metabolites such as tannins, saponins, essential oils, alkaloids and flavonoids which are involved in the healing properties (Ghribia et al., 2014).

A wide range of reports are available on the biological and pharmacological activities of *S. jollyanum*. These include proximate analysis, antidiabetic activity, treatment of benign prostatic hyperplasia (BPH), antioxidant activity, hepatoprotective activity, anti-inflammatory activity, antimalarial activity, haematological activity, anti-allergy activity, antimicrobial activity, antidepressant activity and gastroprotective activity.

3.2.1. Antidiabetic activity

Diabetes is a life-threatening metabolic condition. Chronic hyperglycemia can be caused by a lack of insulin synthesis or a failure of peripheral tissues to respond to the presence of insulin (Geberemeskelet al., 2019). Anti-hyperglycaemic and anti-diabetic activities of *S. jollyanum* petroleum ether seed extracts were evaluated in hyperglycaemic and in alloxan diabetic rabbits.

The petroleum ether seed extract (1 gkg^{-1}*b.w.*) and glibenclamide (10 $mgkg^{-1}$*b.w.*) reduced blood glycemic level by 20% and 43.8% respectively compared with the untreated group. The standard drug used in the experiment was glibenclamide.

In alloxan diabetic animals, treatment with the seed extract of *S. jollyanum* significantly ($p < 0.05$) reduced the blood glucose level in a dose dependent manner from day 3 of daily treatment and continued till the last day of the treatment. Further reduction was however recorded during post-treatment with the extract doses of 300, 600 and 1200 $mgkg^{-1}$*b.w.* showing maximum percentage reduction of 12.3, 29.2 and 32.7 respectively while glibenclamide treated group (10 $mgkg^{-1}$) recorded a reduction of 51.9% (Mbaka et al. 2010).

In addition, Alese et al. (2014) investigated the effects of *S. jollyanum* root methanol extract on blood glucose level in Streptozotocin-induced diabetic rats. The result showed a significant ($p < 0.05$) reduction in blood glucose level in methanol extract and glibenclamide treated groups. Prior to STZ administration, there was no significant difference in the blood glucose level among the *S. jollyanum* extract treated group and glibenclamide treated group. At the end of STZ administration, a significant increase was observed in 200 $mgkg^{-1}$ *S. jollyanum* extract treated group (22.5 $mmolL^{-1}$) and 0.5 $mgKg^{-1}$ Glibenclamide treated group (21.28-22.5 $mmolL^{-1}$).

In a separate experiment, Adeleke et al. (2022) explored how aqueous extracts of the root and leaves of *S. jollyanum* improved wound healing in diabetic rats by regulating pro-inflammatory cytokines, vascular

endothelial growth factor, and microbial colonization. Normal rats were fed a high fat diet for 14 days before receiving an intraperitoneal injection of low dose streptozotocin (35 $mgkg^{-1}$*b.w.*) to induce diabetes (blood glucose > $250mgdL^{-1}$). Wounds were later made, and treatments were given for 14 days. On diabetic rat wounds, oral and topical administration of *S. jollyanum* root and leaf extracts (100 and 200 $mgkg^{-1}$*b.w.*) and the standard drug, silver sulfadiazine significantly ($p < 0.05$) reduced secretion of pro-inflammatory cytokines (TNF-α, IL-6), number of microbial colonies (Colony Forming Unit CFU/mL 10^2), activity of myeloperoxidase, and significantly increased growth factor secretion (Adeleke et al., 2022).

Diabetic rat wound tissues had matured tissue granulation, new blood vessels, collagen, and fibroblasts, and fewer inflammatory cells, according to histological examinations. According to Adeleke et al. (2022), *S. jollyanum* improved wound healing, possibly due to constituents identified by gas chromatography-mass spectrometry (GC-MS) analysis, and thus could be recommended as a therapeutic agent for diabetic wound treatment (Adeleke, 2022). In contrary, the GC-MS is not a valid method to analyse aqueous extract since these are mainly composed of polar (non-volatile) compounds (Brusolti et al. 2014; Venditti, 2018). It is suggested not to take the data on the chemical composition as definitive but be verified by applying the most appropriate analytical methods. Further suitable studies for isolation and characterization of the aqueous extract of this plant is suggested.

3.2.2. Treatment of benign prostatic hyperplasia (BPH)

Benign Prostatic Hyperplasia (BPH) is one of the most frequent urinary illnesses in older men, and it can cause symptoms in the lower urinary tracts (LUTS). Age is one of the most important risk factors for the development of BPH disease. The condition becomes more common as people get older (Csikos et al., 2021). The histomorphological effects of *S. jollyanum* seed on BPH that frequently causes bladder outlet obstruction was examined (Mbaka et al., 2019).

The increase in prostate weight is often considered a reliable index of BPH development. The *S. jollyanum* treated animals showed a dose dependent reduction in 300 and 600 $mgkg^{-1}$ with prostate weight decrease of 79.3% and 89.7% respectively. The standard drug (Finasteride) gave a reduction of 68% at 0.1 $mgkg^{-1}$. The testosterone level was elevated to 5.7 $ngmL^{-1}$ in BPH animals. A dose dependent reduction was observed in *S. jollyanum* extract treated group giving 68.4% (1.8 $ngmL^{-1}$) and 70.2% (1.7 $ngmL^{-1}$) in 300 and 600 $mgkg^{-1}$ respectively. The standard drug, Finasteride decreased testosterone level by 70.2% (1.7 $ngmL^{-1}$).

The petroleum ether extract of *S. jollyanum* seed produced noticeable reduction in prostate weight of rats with BPH with histo-morphology of the tissue showing disintegrated stromal and epithelial cells with rare epithelial involutions of glandular tissue (Mbaka et al., 2019).

3.2.3. Antioxidant activity

Both reactive oxygen and nitrogen species are known to damage lipids, proteins, enzymes, and nucleic acids in living organisms, leading to disorders such as neurodegenerative disease, aging, malaria, atherosclerosis, cancer, diabetes, liver injury, Alzheimer's disease, Parkinson's disease, and other pathological events (Hossai et al., 2019). Numerous constituents in medicinal plants have significant antioxidant activity, including the power to inhibit, minimize, or stop oxidative damage to nucleic acids, lipids, and proteins, as well as other cellular constituents (Sousa et al., 2014). The antioxidant activity of different organs of *S. jollyanum* extracts were evaluated using 2,2-diphenyl-1-picrylhydrazyl radical (DPPH) (Nia et al., 2004). The leaf extract gave a weak activity (IC_{50} 4.35 μgmL^{-1}) followed by the root bark (3.50 μgmL^{-1}). The most active was the chloroform fraction of the stem bark (IC_{50} 1.54 μgmL^{-1}). The standard drug, ascorbic acid gave IC_{50} 0.80 μgmL^{-1}). The antioxidant (*in vitro*) activity of *S. jollyanum* stem extract was also assessed with radical scavenging of superoxide and hydrogen peroxide (H_2O_2) which displayed significant antioxidant activity (Olorunnisola et al., 2011). The methanol stem extract was screened for superoxide radical scavenging and hydrogen peroxide radical scavenging potentials. The study showed antioxidant activity with values of IC_{50} 13.11 μgmL^{-1} and 30.0 μgmL^{-1}, respectively. The standard drug, ascorbic acid gave the IC_{50} values of 15.34 $\mu gmL^{-1}$and 35.44 μgmL^{-1}respectively.

To validate the therapeutic potential of *S. jollyanum* leaves, Uka et al. (2020) investigated the phytochemical components, acute toxicity, and antioxidant activity of the ethanol extract. Total phenolic, flavonoid content, DPPH radical scavenging activity, ferric reducing antioxidant power (FRAP), and iron chelating activity were all used to assess antioxidant activity *in vitro* using standard protocols. Alkaloids, saponins, tannins, flavonoids, and cardiac glycosides were among the phytochemical contents, with total phenolic, flavonoid, and gallic acid equivalents of 31.49, 29.98, and 1215.80 $mgmL^{-1}$, respectively.

In addition, the acute toxicity of the ethanol extract of *S. jollyanum* leaves on albino mice showed the LD_{50} to be beyond 4743.42 $mgkg^{-1}$*b.w.* For DPPH, FRAP, and iron chelating activities, the leaf extract of *S. jollyanum* had IC_{50} values of 164.214, 72.410, and 167.202 $mgmL^{-1}$, respectively. The standard drug, ascorbic acid had IC_{50} values of 248.081, 155.134, and 270.703 $mgmL^{-1}$, for DPPH, FRAP, and Iron chelating activities respectively. The findings show that the extract is high in antioxidant components and has numerous pathways for eliciting antioxidant effects, providing a scientific foundation for its usage in traditional medicine (Uka et al., 2020).

3.2.4. Hepatoprotective activity

Antioxidant properties, improved antioxidant defense (superoxide dismutase, catalase, and glutathione peroxidase activity), reduced peroxidation, anti-inflammatory activity and attenuation of many

inflammatory processes, anti-fibrotic properties of plants, and stimulation of extracellular matrix degradation are all mechanisms that medicinal plants use to protect the liver (Al-Snafi et al., 2019). The methanol crude extracts; 50, 100 and 200 mgkg^{-1} were given orally to Wistar rats, and the hepatotoxicity was induced by administering 30%, 1.0 mLkg^{-1} CCl_4 (Olorunnisola et al., 2011). Olive oil (1.0 mLkg^{-1}*b.w.*) was administered as the control. The extract displayed a good hepatoprotective activity against CCl_4 induced total protein and antioxidant markers depletion in liver. The extract returned the activity of the marker enzymes to almost normal. The study revealed that *S. jollyanum* extract had excellent hepatoprotective activity against CCl_4-induced liver damage. This activity could be due to the strong antioxidant property (Olorunnisola et al., 2011).

3.2.5. Anti-inflammatory activity

Inflammation is a universal process that occurs in a disturbed state of homeostasis, such as damage, exposure to contaminating substances, and infection, and is initiated by innate immune system receptors to remove pathogens when they are identified (Sami et al., 2021).

Moody et al. (2005) investigated the *in vivo* anti-inflammatory activity of *S. jollyanum* methanol crude extracts using carrageenan-induced hind paw oedema of orally administered albino rats. In healthy adult Wistar rats, the methanol fruit extract gave a higher activity (79.58% inhibition) at a concentration of 200 mgkg^{-1} when compared with root extract which gave 53.75% inhibition at 200 mgkg $^{-1}$. The reference drug acetylsalicylic acid gave percentage inhibition of 72.5% at 100 mgkg^{-1}. The fruit methanol extract was the most active and further purified to give three clerodane diterpenoids; columbin, isocolumbin, fibleucin (Moody et al., 2005), which were also screened for anti-inflammatory activity. Out of the three isolated compounds, columbin was found active with 67.08% inhibition at 20 mgkg^{-1} ($p < 0.05$) (Moody et al., 2005).

In addition, Fadahunsiet al. (2018) evaluated the anti-inflammatory potential of *S. jollyanum* leaf. The anti-inflammatory activities of the leaf were assessed using the inhibitory effect of the extracts on erythrocyte membrane stabilization, trypsin, and lipoxygenase (*in vitro*). The changes in optical density of test samples and controls were measured and inhibition was determined using a 96-well micro plate reader Spectra Max 384 plus (Molecular Devices, USA). The aqueous extract and saponin rich fraction had the highest dose dependent erythrocyte membrane stabilizing capacity among the crude and secondary metabolites rich extracts. With an IC_{50} of 637 µgmL^{-1}, the aqueous extract showed a significant ($p < 0.05$) dose-dependent lipoxygenase inhibitory activity when compared to other extracts. The standard drug, diclofenac gave the IC_{50} of 52 µgmL^{-1}. In the proteinase inhibitory assay, the ethanol and tannins rich fractions had the highest inhibitory capacity, with IC_{50} values of 840 and 1810 µgmL^{-1}, respectively, among the crude and fractions. Indomethacin was used as a standard, with an IC_{50} of 246 µgmL^{-1}. These findings give scientific evidence to support the traditional therapeutic usage and suggest that the *S. jollyanum* plant could be used to develop anti-inflammatory agents (Fadahunsi et al., 2018).

Similarly, Carrageenan-induced paw oedema, egg albumin-induced paw oedema, and xylene-induced ear oedema were used to test the anti-inflammatory activity of the ethanol leaf extract of *S. jollyanum* (ELESJ) in mice *in vivo* at dosages of 474.34, 948.68, and 1423.03 mgkg^{-1}*b.w.*, respectively (Uka et al., 2021). The extract caused significant ($p < 0.05$) dose-dependent and time-dependent reductions in mean paw thickness, according to the findings. Similarly, at the maximum dose (1423.03 mgkg^{-1}), the extract showed a dose-dependent rise in percentage inhibition of carrageenan and egg-albumin-induced paw oedema (34.49% and 36.71%, respectively), comparable to the anti-inflammatory effects of the standard drug acetylsalicylic acid (34.69%, 31.54%). In comparison to the control and standard groups, the extract elicited significant ($p < 0.05$) dose-dependent reductions in xylene-induced ear oedema weight in all test groups.

Furthermore, at the highest dose (1423.03 mgkg^{-1}), the extract showed a dose-dependent percentage inhibitory effect (44%) comparable to that of the reference drug, dexamethasone (48%) at 4 mgkg^{-1}. The reference drug is found to be more effective when compared with *S. jollyanum* extract considering a wide margin in the doses. The findings of this study support the use of *S. jollyanum* leaf extract in folk due to its considerable anti-inflammatory property, which could be linked to the leaf's phytochemical contents (Uka et al., 2021).

3.2.6. Anti-malarial activity

The anti-plasmodial activity of *S. jollyanum* leaf and root methanol extracts were reported by Olorunnisola and Afolayan (2011). Anti-plasmodial activity of the methanol extract was assessed *in vitro* using Swiss albino mice inoculated with chloroquine-resistant Plasmodium berghei NK67 strain. The two extracts showed considerable dose-dependent antiplasmodial activity in isolation as well as in combination with elevated average survival time in the four-day curative standard test. The standard drug: Arthemeter-Lumefartrin at 5 mg gave the maximum antimalarial activity with 81.4% inhibition; the leaf extract at 200 mg gave 74.7%, while the root extract at 200 mg showed 54.1% anti-malarial activity. The two extracts also had a beneficial impact on the weight of treated animals and hematology values. The promising antiplasmodial activity displayed by the plant extract could be due to the plant's phytochemicals. The study also found that the leaf and root of *S. jollyanum* have efficient anti-malarial activity against chloroquine-resistant strain. This confirmed the traditional claim that *S. jollyanum* extract was used in malaria management (Olorunnisola and Afolayan, 2011).

3.2.7. Haematological activity

When certain blood parameters are increased above their typical values, hematotoxicity develops. Because red blood cells have unsaturated membrane lipids, they are particularly vulnerable to lipid peroxidation (Enenebeaku et al., 2021).

S. jollyanum methanol extracts (leaf and root) were tested with chloroquine-resistant Plasmodium berghei NK 67 for haematological activity using wistar mice. The extracts were given to the mice for 7 days in a row. The outcome acquired showed an increase in the pack cell volume (PCV) and mean corpuscular volume (MCV). Except for neutrophils and monocytes, the red and white blood cells also increased. Therefore, the study indicates that the extract stimulated hematopoietic stem cells (Mbaka et al., 2010).

Wopara et al. (2019) also investigated the effect of ethanol root extract of *S. jollyanum* on some haematological test parameters of Wistar rats using automated haematological analyzer systemex KX-21 (Japan). The administration of 200 $mgkg^{-1}$ of *S. jollyanum* extract caused a reduction in the PCV which is contrary to the result of Mbaka et al. (2010) which showed an increase in the PCV. The haematological activity of this plant therefore requires further research.

3.2.8. Anti-allergy activity

The hyper-sensitivity of immune system to non-infectious stimulation in the environment is characteristic of allergic disorder which could be detrimental reactions to the host. Allergic disorders include eczema, bronchial asthma, inflammatory bowel disease, allergic rhinitis. Over 300 million people are affected by these illnesses and 1 in every 250 fatalities worldwide. The anti-allergic activity of *S. jollyanum* fruit extract was evaluated in milk induced eosinophilia and leukocytosis in mice (Olorunnisola et al., 2017). The ethanol fruit extract and the standard drug, dexamethasone demonstrated a considerable dose-dependent decrease in the absolute eosinophil and lymphocyte counts. The results suggested the anti-allergy property of the *S. jollyanum* fruit extract, and the mode of activity may involve multiple mechanisms as a result of phytochemical interactions (Olorunnisola et al. 2017).

3.2.9. Antimicrobial activity

Antimicrobial resistance (AMR) is the ability of microorganisms like bacteria and fungi to develop despite being exposed to antimicrobial (antibacterial or antifungal) agents that are supposed to stop them from growing (Anyanwu et al., 2017). In general, bacteria display AMR by innate (*e.g.*, lack of drug target site) and/or acquired (*e.g.*, enzymatic drug degradation) processes imparted by AMR genes (ARGs) acquired from other microorganisms *via* horizontal gene transfer (HGT) (transformation, transduction, and conjugation) (Anyanwu et al., 2017).

The antimicrobial activity of crude methanol leaf extract of *S. jollyanum* was previously evaluated by Udoh et al. (2021). *Fusarium* species were isolated and identified using standard mycological techniques. Using modified agar well diffusion and modified agar disc diffusion methods, the extract, and antifungal agents (miconazole, ketoconazole, terbinafine, fluconazole, ciclopirox, voriconazole, and itraconazole) were tested against 1,260 and 2,140 fusarial isolates from human and plant specimens, respectively.

S. jollyanum extract exhibited significant antifungal action against both human and plant isolates tested, according to a susceptibility test. The extract's mean inhibition zone diameter (IZD) against isolates from human and plant sources was 31.97 ± 0.66 and 29.03 ± 0.97, respectively, while voriconazole (most potent) had inhibition zone diameters of 15.48 ± 0.69 and 15.24 ± 0.70 for human and plant isolates, respectively. Fluconazole was next, with an IZD of 13.76 ± 0.78 for humans and 13.99 ± 0.81 for plants, respectively. The activity of the extract was significantly different from that of antifungal drugs (p = 0.000). *S. jollyanum* had the lowest minimum inhibitory concentration (MIC) of 0.0679 μgmL^{-1}, while antifungal agents had an MIC < 1. The findings of this study therefore revealed that *S. jollyanum* is a rich source of antimicrobial (antifungal) agent (Udoh et al., 2021).

In addition, the antimicrobial activity of *S. jollyanum* extract on *Salmonella typhi* was evaluated using agar well diffusion method. The crude extract showed a broad-spectrum antibacterial activity, inhibiting the *Salmonella typhi* (Koleosho et al., 2013).

3.2.10. Antidepressant activity

Depression is a broad term for a variety of mental health issues defined by a lack of positive influence, a lack of interest, and mood disturbances that impair cognition and psychomotor performance (Pardhe et al., 2020). Sorrow and sadness are common human emotions; everyone experiences them, but they don't endure long. Major depression, on the other hand, is characterized by a prolonged period of intense despair (Elozia et al., 2017).

The ethanol extracts of *S. jollyanum* roots were studied for antidepressant activity. Two depression animal models forced swimming test (FST) and tail suspension test (TST) were recorded. The immobility duration in both FST (ED_{50} 296.20 ± 53.97 $mgkg^{-1}$) and TST (203.90 ± 39.01 $mgkg^{-1}$) was reduced dose-dependently by the extract at 100-1000 $mgkg^{-1}$. Two standards; imipramime and fluocetin were used. The result showed that *S. jollyanum* is an effective antidepressant drug which can be further purified to serve as drug discovery (Woode et al., 2009).

3.2.11. Acute oral toxicity study and gastroprotective activity

The acute oral toxicity study and the gastroprotective effect of methanol extracts of *S. jollyanum* in Wistar rats were evaluated by Akinwumi et al. (2022). The method of Lorke (1983) was used for acute toxicity study. For

the gastroprotective activity, animals were grouped and pre-treated with varied doses of *S. jollyanum* methanol extracts (50, 100 and 200 mgkg^{-1}) and standard drug (cimetidine 100 mgkg^{-1}) for 7 days and gastric ulcer was induced experimentally using 40 mgkg^{-1}*b.w.* indomethacin on day 8 of treatment. The gastric ulcer index, biochemical and histological evaluation were investigated.

Single dose oral administration of 10, 100, and 1000 mgkg^{-1}*b.w.* of *S. jollyanum* crude extract appeared to be safe visually as no death or noticeable signs of toxicity were observed in treated animals for the first 24 h and by the end of 48 h observation. No late toxicological effect was observed up to 14 days after treatment. However, the kidney, heart and liver were affected in high dosages of 1600, 2900 and 5000 mgkg^{-1} treated rats. This plant should therefore be used cautiously as a treatment for ailments.

Cimetidine (100 mgkg^{-1}*b.w.*), *C. pilosa* (50 mgkg^{-1} *b.w.*), and *S. jollyanum* (200 mgkg^{-1}*b.w.*) gave inhibitions of 97.5%, 82.5%, and 72.5% respectively, compared to 0% of the ulcer untreated. A significant increase in antioxidant parameters was observed compared with ulcer untreated group.

S. jollyanum methanol extract demonstrated gastroprotective activity probably *via* increased antioxidant activity against indomethacin induced gastric ulcer thereby justifying the ethnomedicinal claim (Akinwumi et al., 2022).

3.2.12. Assessment of reproductive toxicity

The effect of hydroethanolic root extract of *S. jollyanum* on reproductive function was studied in male Sprague Dawley rats using Plasma testosterone, follicle-stimulating hormone, and luteinizing hormone assays (Baffoe et al., 2021). These plants' roots have been used frequently in polyherbal preparations to achieve maximum results. On repeated use, it was discovered that the hydroethanolic root extract of *S. jollyanum* had a negative impact on reproductive function. Therefore, using this plant frequently could result in male infertility, making them unsafe for healthy males who desire to have children (Baffoe et al., 2021).

3.2.13. Toxicity and mutagenicity

The toxicity of *S. jollyanum* was evaluated using Fischer 344 male rats and the genotoxic effect of the alcoholic extract of the roots (Amidu et al., 2008). The result revealed that the no-observed adverse effect level (NOAEL) of *S. jollyanum* extract was > 1000 mgkg^{-1}*b.w.* per day in rats which can be regarded as virtually non-toxic. Because the extract induces a drug-metabolizing enzyme, it should only be used cautiously as a treatment for ailments.

4. Phytochemistry

Several isolated natural compounds have so far been reported in the scientific literature using the traditional natural product extraction and purification methods (Walsh et al., 2017).

Phytochemical screening of *S. jollyanum* showed the presence of terpenes, saponins, alkaloids and tannins in the various fractions of the stem bark methanol extract (Nia et al., 2004). The essential oil of *S. jollyanum* root was analyzed by Aboaba and Ekundayo, (2010) using gas chromatography-mass spectrometry (GC-MS) analysis. In total, 19 compounds were obtained, including camphene, δ-3-carene, globulol, 5-guaiene-11-ol, *p*-cymene, α-eudesmol, β-pinene (Fig. 2). The proximate seed extract analysis gave the content of crude protein, moisture, carbohydrates, ash, crude fat and fiber as 48.1, 16.7, 48.1, 16.8, 9.7, and 5.5 percent, respectively, with an energy value of 1460 kcal/100 kg. The isolated compounds comprise monoterpenoids (33.5%) and sesquiterpenoids (56.3%), while the remaining 10.2% were unknown.

Moody et al. (2005) isolated three clerodane diterpenes; columbin, isocolumbin, and fibleucin from the fruits of *S. jollyanum* (Fig. 3). The fruits of *S. jollyanum* were collected at the University of Ibadan, Nigeria. Authentication was done at Forest Herbarium Ibadan (FHI) where voucher specimen FHI 105364 was deposited. It was shade dried and pulverized. Extraction (2 kg) was carried out using cold percolation method with methanol for 72 h. The extract was filtered and evaporated using rotary evaporator under reduced pressure to give 84.2 g. The MeOH fruit extract (10 g) was subjected to silica gel vacuum liquid chromatography using *n*-hexane with an increasing percentage of ethyl acetate and then methanol as eluents. Further purification using preparatory thin layer chromatography resulted in isolation of three clerodane diterpenes namely columbin (**1**), isocolumbin (**2**) and fibleucin (**3**). Columbin (67.08% inhibition at 20 mgkg^{-1}, $p < 0.05$) gave significant anti-inflammatory activity when compared with reference acetylsalicylic acid (72.50% inhibition at 100 mgkg^{-1}).

Biological activities of clerodane diterpenes include insect antifeedant activity, antifungal, antitumor, antibiotics, anti-ulcer, hypoglycemic, antiplasmodial, hypolipidemic, and antithrombin inhibitory activities. Clerodane diterpenes are well-known for their insect antifeeding and insecticidal properties, highlighting the safety of such natural insect antifeedants for fish and mammals. Over 400 natural and semi-synthetic clerodanes were evaluated using various laboratory experiments to produce several compounds with strong antifeedant activity against numerous classes of insects (Li et al., 2016). Camphene is a bicyclic monoterpene and a major component of plant-based essential oil. It is used for fragrance preparation and as artificial flavoring food additives. It is also used in camphor and insecticides manufacturing. It has also been shown to have a protective impact against oxidative stress (Tiwari et al., 2009).

Essential oils generally function as antibacterial agents against a broad variety of pathogenic bacterial strains such as *Listeria innocua, Listeria monocytogenes, Bacillus cereus, Staphylococcus aureus,* etc. In addition to the use of essential oils as natural sanitizing agents in the food industry, antimicrobial activity such as minimum

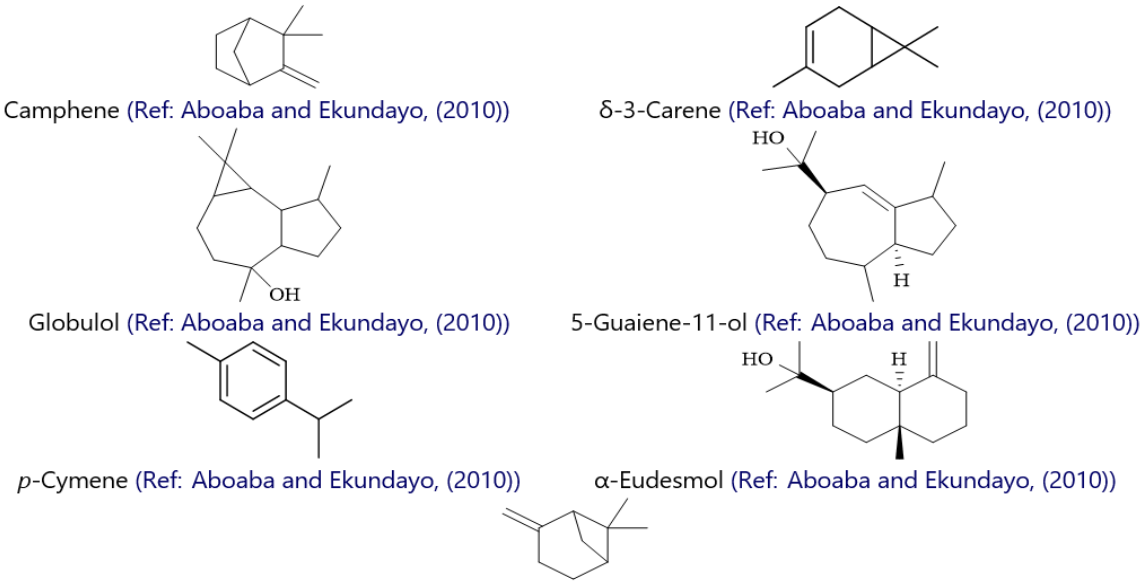


Fig. 2. Isolated compounds from the essential oil of *Sphenocentrum jollyanum*.

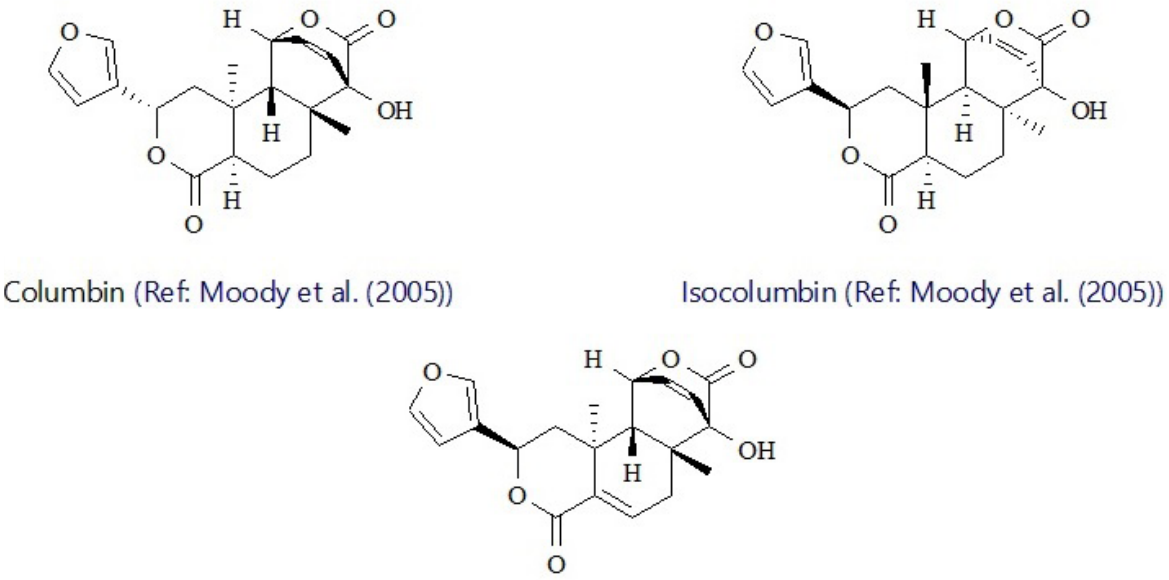
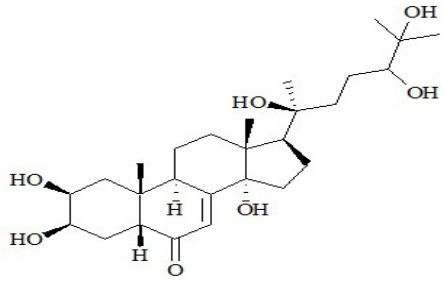
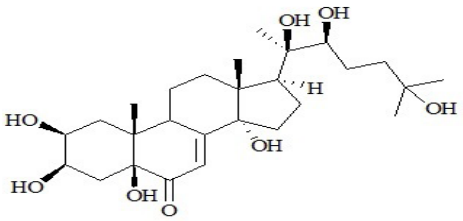


Fig. 3. Isolated clerodane diterpenes from *Sphenocentrum jollyanum* seeds.

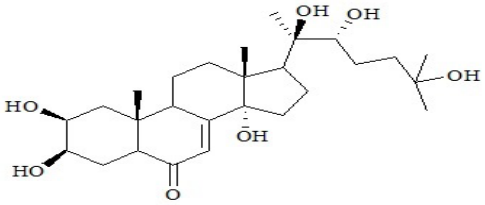
inhibitory concentration (MIC), mycelial growth inhibition and minimum fungicidal concentration (MFC) of six essential oils against *Penicillium chrysogenum, Aspergillus terreus, Aspergillus niger, Chaetomium globosum, Penicillium pinophilum, Trichoderma viride* and *Trichoderma harzianum* was also evaluated (Angelini et al., 2008). The antimicrobial activity was monitored using microdilution method and a wide spectrum of antimicrobial activities was exhibited in the essential oil. Essential oils are also rich in phenolic compounds thus attracting scientists to evaluate their antioxidant activity. Furthermore, Akinwumi et al. (2021) isolated five known ecdysteroid compounds from *S. jollyanum* ethyl acetate and *n*-butanol fractions. These are pinnatasterone, polypodine B, 20-hydroxyecdysone, 20,26-dihydroxyecdysone, and atrotosterone A (Fig. 4).



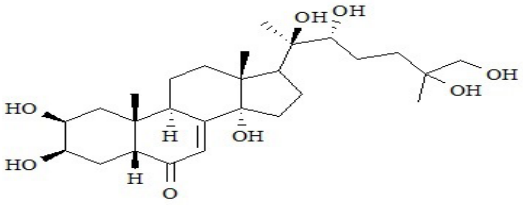
Pinnatasterone (Ref: Akinwumi et al. (2020))



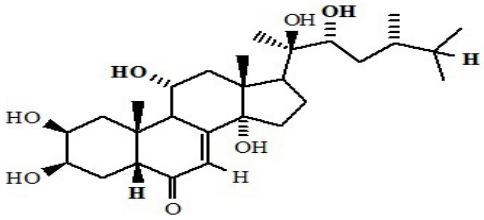
Polypodine B (Ref: Akinwumi et al. (2020))



20-hydroxyecdysone (Ref: Akinwumi et al. (2020))



20,26-dihydroxyecdysone (Ref: Akinwumi et al. (2020))



Atrotosterone A (Ref: Akinwumi et al. (2020))

Fig. 4. Isolated ecdysteroids from *Sphenocentrum jollyanum* seeds.

S. jollyanum seeds were collected at their local habitat in Odo ona area, Apata, Ibadan, Nigeria. Plant identification and authentication was done at Forest Herbarium, Ibadan (FHI), with FHI number 110510. The dried seeds were shade dried for three weeks and then pulverized. The powdered sample was extracted with 100% methanol. A part (200 g) of the extract was next dissolved in MeOH: H_2O and then partitioned with *n*-hexane, dichloromethane (DCM), EtOAc and *n*-butanol. The filtrates were evaporated *in vacuo* at 40 °C. The EtOAc soluble fraction (15 g) was packed on silica gel column (length: 75 cm, diameter: 17 cm). Further purification with preparative TLC gave atrotosterone A (**5**). Pinnatasterone (**1**) was eluted as a pure compound at 10% MeOH in DCM from the column. The *n*-butanol-soluble fraction (15 g) was loaded on to a column silica gel to give three compounds; polypodine B (**2**), 20-hydroxyecdysone (**3**) and 20,26-dihydroxyecdysone (**4**) after further purification with reversed phase preparatory HPLC.

Extensive 1D and 2D NMR experiments were used to determine the structures of the compounds, and FAB-MS was used to confirm their molecular masses. The five isolated ecdysteroids have 6-keto,7-ene conjugated system in common; all the compounds are similar in the steroidal part except for polypodine B and atrotosterone A, which have hydroxyl function at C-5 and C-11, respectively. The major difference in the structure is the side chain.

Ecdysteroids are polyhydroxysteroids with an A/B ring junction and a 14α-hydroxy-7-en-6-one configuration (Yingyongnarongkul and Suksamrarn, 2000).

The urease inhibitory and antacid properties of the five compounds were investigated. Polypodine B, 20-hydroxyecdysone and pinnatasterone showed significant urease inhibitory activity (IC_{50} 7.0 ± 0.56, 13.8 ± 0.49 and 14.1 ± 0.59), respectively. The urease inhibitory activity of 20,26-dihydroxyecdysone (IC_{50} 24.1 ± 1.21) and atrotosterone A (IC_{50} 29.3 ± 7.45) were moderate compared to that of acetohydroxamic acid (IC_{50} value 20.3 ± 0.43) at the same concentration of 0.5 mM (Akinwumi et al., 2021).

Similarly, the phytochemical investigation of the ethyl acetate fraction of *S. jollyanum* root yielded six compounds: two new phytoecdysteroidal glycosides, sphenocentroside A and sphenocentroside B (Fig. 5), and four known phytoecdysteroids, polypodoaurein, polypodine B, ecdysterone, and

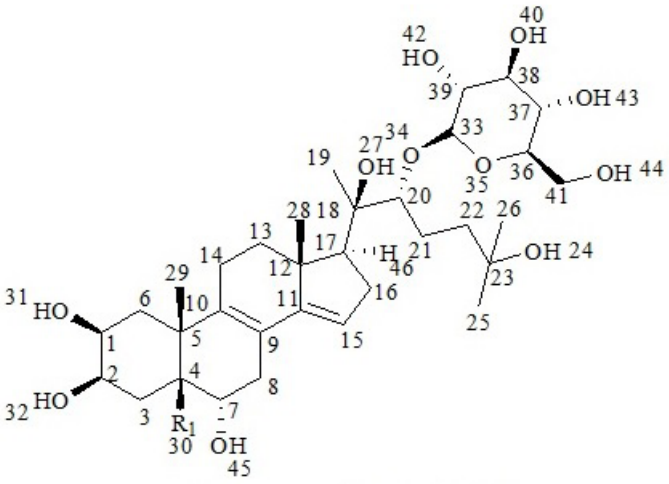


Fig. 5. Two new phytoecdysteroidal glycosides from *Sphenocentrum jollyanum* (Ajayi et al., 2019).

20,26-dihydroxyecdysone. The roots of *S. jollyanum* were obtained from Itak Ikot Akap in Ikono Local Government Area of Akwa Ibom State, Nigeria 2017. The plant was authenticated at Forest Herbarium Ibadan (FHI), Nigeria where voucher specimen was deposited with FHI number 111156. The roots were air dried and pulverized, the powdered roots (8 kg) were extracted in 70% MeOH for 72 h. The filtrate was concentrated to dryness. The methanol extract (100 g) was suspended in MeOH-water (1:3), fractionated with EtOAc and evaporated *in vacuo* to yield 22.2 g. The ethyl acetate fraction (5 g) was loaded on a 100 g silica gel column. Elution with DCM and MeOH mixtures in increasing polarities yielded 23 fractions (A1-A23).

Fraction A10 (500 mg) was further purified on a sephadex column (100 g) using MeOH as eluent, to afford polypoduarein. Further silica gel column chromatography purification of fractions A13 (450 mg), A16 (575 mg) and A20 (400 mg), separately over silica gel column and DCM-MeOH as eluents in increasing polarities to afford polypodine B, ecdysterone and sphenocentroside A, respectively. Fraction A22 (380 mg) was purified using sephadex column (100 g), with MeOH as eluent and afforded sphenocentroside B and 20,26-dihydroxyecdysone.

The compounds were identified by their Nuclear Magnetic Resonance (NMR), Infrared Spectroscopy (IR) and Mass Spectroscopy (MS). A novel steroidal glycoside was produced as a white solid, and its HR-ESIMS analysis revealed a sodiated molecular ion peak at *m/z* 649.3587[M +Na]$^+$, which corresponds to seven degrees of unsaturation (the calculated value for $C_{33}H_{54}O_{11}Na^+$ is 649.3565).Compound 2 was also obtained as a white solid, and its HR-ESIMS revealed a sodiated molecular ion peak at *m/z* 665.3536 [M+Na]$^+$ (Calcd for $C_{33}H_{54}O_{12}Na^+$ is 665.3514), indicating 7 degrees of unsaturation and differing from 1 by an additional oxygen. Only sphenocentroside B, a novel compound, exhibited a moderate antimicrobial activity of 51% against *E. coli* at a concentration of 20 µgmL^{-1}(Ajayi et al., 2019). However, the value of the positive control was not reported thereby making it difficult to make comparison.

5. Proximate analysis

Proximate and elemental analyses of medicinal plants are methods of profiling them in order to detect the chemical and element classes present, which are all linked to their use and authenticity. These elements and compounds are responsible for the nutritional and therapeutic properties of plants (Quadri et al., 2021).

The dry root sample and ethanol root extract of *S. jollyanum* were analyzed for proximate constituents such as protein, moisture, carbohydrate, fibre, ash, and fat, as well as quantitative phytochemical constituents such as tannins, alkaloids, phenols, flavonoids, terpenoids, and steroids (Ekpono et al., 2018). The results showed the presence of phytochemicals such as terpenoids, flavonoids, steroids, tannins, alkaloids, phenols and proximate composition (percent) revealed the presence of fat (2.6%), protein (7.3%), ash (3.4%), moisture (6.3%), fiber (2.8%), and carbohydrate (77.2%) in the ethanol root extract of *S. jollyanum*. According to this research, *S. jollyanum* root could be used as a nutritional supplement as well as a source of antioxidant phytochemicals (Ekpono et al., 2018). Similarly, standard protocols were used to assess the nutrient and antioxidant properties of *S. jollyanum* oil. Unsaturated fatty acids made up 48.3% to 57.0% of the oil. Lunamarine, kaempferol, and catechin were found to be the most abundant phytochemicals in the oil. The

oil also had a high antioxidant activity (Agomuo and Uchenna, 2018).

6. Chemotaxonomic relevance

Chemotaxonomy, also referred to as chemical taxonomy, is a branch of biology that classifies plants based on their chemical composition. All living organisms produce secondary metabolites, which are created from primary metabolites (Singh, 2016). Malvaceae, Ranunculaceae, Magnoliaceae, Polygonaceae, and Solanaceae are some of the more well-known plant families that have been investigated for chemotaxonomy (Sivarajan, 1991). However, numerous plant species from various families as well as organisms from other taxonomic groups have been found to have a broad family of secondary metabolites known as clerodane diterpenoids. These compounds have attracted interest in recent years due to their remarkable biological activities, particularly insect antifeedant effects (Li et al., 2016).

Clerodane diterpenoids have been isolated and identified from several families including Euphorbiaceae (*Croton*), Lamiaceae (*Cornutia*, *Salvia* and *Teucrium*), Olacaceae (*Ptychopetalum*), Sapindaceae (*Dodonaea*) and Scapaniaceae (*Scapania*). In Menispermaceae family, previous report showed that clerodane diterpenoids are most abundant in the genus *Tinospora*. These compounds were previously isolated from *Tinospora cordifolia* (Sivasubramanian et al., 2013), and *Tinospora sagitata* (Li et al. 2016; Zhang et al., 2016). Also, clerodane diterpenoids (columbin and isocolumbin) have been previously reported in species such as *Penianthus zenkeri* Diels (Achenbach and Hemrich, 1991; Tane et al., 1997), *Burasaia madagascarensis* DC. (Mambu et al., 2002), *Burasaia congesta* Decne, *Burasaia gracilis* Decne and *Burasaia australis* Elliot (Rasoanaivo et al., 1991), which all belong to the family Menispermaceae.

Many compounds have been isolated from various organs of *S. jollyanum*. From the context of this review, it is discovered that *S. jollyanum* from Menispermaceae is a good source of clerodane type diterpenoids and ecdysteroids. Also, there are reports of ecdysteroids in various Menispermaceae species. One of the most common and abundant ecdysteroids, 20-hydroxyecdysone isolated from *S. jollyanum* has been previously reported in *Serratula coronata* L. (Odinokov et al., 2002), *Serratula tinctoria* L. (Rudel et al., 1991), *Silene claviformis* Litv. (Sadikov et al., 2001), *Leuzea carthamoides* (Willd.) DC. (Budesinsky et al., 2001) and *Penianthus longifolius* Miers (Tabekoueng et al., 2019). It is concluded that the plant family Menispermaceae is a good source of ecdysteroids. Sphenocentroside A and sphenocentroside B are first isolated from *S. jollyanum* from a chemotaxonomic standpoint.

7. Concluding remarks and future prospects

The current review established the increasing importance of *S. jollyanum* in traditional medicine and medicinal plant research. The detailed information about the traditional uses, phytochemistry and pharmacological importance of *S. jollyanum* were reported.

The various organs of the plant are used traditionally for the treatment of several ailments. The fruits and roots are used for treatment of gastric ulcer when ground into powder. The aerial part is also used for treating coughs and fever. The extracts of this plant also possess anti-diabetic, antioxidant, anti-inflammatory, anti-depressant and haematological activities. The phytochemical screening of *S. jollyanum* revealed the presence of terpenes, saponins, alkaloids and tannins in the various fractions of the stem bark methanol extract. *S. jollyanum* is found to be rich in terpenoids (diterpenoids) and ecdysteroids. Plant ecdysteroids are present in several groups of angiosperms; several ecdysteroid-containing medicinal plants are beneficial in many ways with reported pharmacological activities. The compounds present in this plant could be responsible for its various pharmacological activities.

Toxicity is observed in some of the reported studies, these studies deserve further in-depth studies to identify the responsible compounds and for secure use of this medicinal plant in traditional medicine.

It is important to note that not all the organs used traditionally are reported for the biological activities. For instance, the aerial part is traditionally used for treatment of coughs and chronic injuries, the morphological organs are used in the local treatment of sickle cell disease, the roots are locally used in managing hypertension and breast tumor. It is recommended that future research activities focus on biological activities such as antitubercular, wound healing, antisickling, antihypertensive and anticancer activities. This will confirm the efficacy and safety of the plant

It is also recommended that future research activities focus on isolation and characterization of compounds from *Sphenocentrum jollyanum* and plant family Menispermaceae to possibly isolate other classes of compounds. The isolated compounds can therefore be screened for various biological activities. For compound isolation and the discovery of new substances from this amazing medicinal plant, chromatography techniques such as thin layer chromatography (TLC), high performance liquid chromatography (HPLC), mass spectrometry (MS), and nuclear magnetic resonance (NMR) are essential. The chemotaxonomy of this important species and the family Menispermaceae is also recommended, the result will be valuable to plant taxonomy in the future.

Conflict of interest

The authors declare that there is no conflict of interest.

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