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Original Research Article

High Performance Liquid-Chromatography Profiling of *Swietenia mahagoni* Stem Bark Crude Extract of and their Pharmacological Importance in Benign Prostatic Hyperplasia Management

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ABSTRACT

Benign prostatic hyperplasia or BPH, is a condition characterised by progressive prostate enlargement and lower urinary tract symptoms (LUTS) in ageing men. Orthodox drugs such as α-blockers and 5α-reductase inhibitors are effective but limited by adverse effects, particularly sexual dysfunction. This study was to screen the bioactive compound in ethanol stem bark crude extract of *Swietenia mahagoni* using HPLC. A total of 20 compounds were detected; including phytosterols, flavonoids, limonoids, alkaloids and sesquiterpenes which are known to be candidates in BPH and related disorders mangements. Current evidence strongly supports stigmasterol and β-sitosterol as the most advanced candidates, as both inhibit 5α-reductase, reduce dihydrotestosterone (DHT) and androgen receptor (AR) expression, relieve prostatic smooth muscle contraction, and induce apoptosis. Among flavonoids, quercetin, kaempferol and epicatechin gallate has been reported as potential anti-hyperplastic effects through 5α-reductase inhibition, Nrf2 modulation and anti-inflammatory actions. The limonoids swietenine and swietenolide activate Nrf2/HO-1 and suppress NF-κB and NLRP3 inflammasome pathways. Several compounds – lucenin, rhamnetin, swietephragmin H, melionine, germacrene D, swietmahonin, swiettenitin and oxalic acid,lack direct BPH evidenc. We propose a translational roadmap that prioritises stigmasterol for early clinical trials, validates swietenine and swietenolide in testosterone-induced BPH rodents, and develops rational multi-compound formulations targeting hormonal, inflammatory and oxidative pathways.

Keywords: Swietenia mahagoni, HPLC profiling, Pharmacological importance benign prostatic hyperplasia

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Introduction

Benign prostatic hyperplasia (BPH) is a common condition caused by the proliferation of prostatic cells, leading to an increase in prostate size, urethral obstruction, and lower urinary tract symptoms.[1] The condition affects 60% of males between aged 50 and 60 years. The symptoms of BPH can include discomfort during urination and may lead to complications such as recurrent urinary tract infections (UTIs) and renal failure.[2] The common risk factors for BPH include increasing age, functioning testicles, metabolic syndromes, family history of BPH, obesity, history of diabetes, and black race.[3] Pathophysiologically, BPH occurs in the prostate's transitional zone, where stromal and epithelial cells interact. The growth of these cells is affected by sex hormones and cytokine responses. Within the prostate, testosterone is converted to dihydrotestosterone (DHT), where androgen is thought to be the main mediator of prostatic hyperplasia.[4] The role of DHT was demonstrated when men with BPH were found to have significantly higher DHT levels within prostate tissue compared to men whose prostates were of normal size.[5]

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The clinical importance of DHT became clear when patients treated with orchiectomy and 5-alpha-reductase inhibitors showed decreases in BPH symptomatology as DHT decreased. The factors associated with worsening disease progression include old age, severe lower urinary tract symptoms, increased prostate size, and high prostate-specific antigen (PSA) levels.[5]

Recently, benign prostate hyperplasia has been of great interest to researchers due to the adverse effects of BPH medications on the patients and the high cost of the medications. Phytomedicine has been of used traditionally to manage various health conditions due to the ease of accessibility and less toxic effects compared to standard medications. Hence, the need to explore the use of phytomedicine for the treatment of BPH.

Swietenia mahagoni, also known as West Indian mahogany, belongs to the mahogany family Meliacea .[6.] This family includes about 50 genera and 550 species, mostly found in tropical regions worldwide.[7] Within the genus *Swietenia*, three main species are recognized: *S. mahagoni*, *S. macrophylla*, and *S. humilis*.[8] *Swietenia mahagoni* is a medium-sized tree that can grow25 meters, although some trees in plantation settings have been documented reaching up to 30 meters [6,9]. The trunk diameter can be up to 4 meters wide, and often has short, flat roots at the base. The bark is reddish-brown and scaly on older trees, while younger trees have smooth, greyish bark.[10] The leaves are alternate and compound, typically 12-25 cm long, and have 8-12 leaflets arranged in 2-5 pairs. Each leaflet is often asymmetrical, with pointed tips.[9, 10]

Research has shown that *Swietenia mahagoni* is rich in phytochemicals, which have potential healing effects against various diseases.[11, 12.] The plant's stem-bark extract contains a high amount of flavonoids, alkaloids, phenols, terpenoids and other compounds such

as vitamins and minerals.[10] Its seeds, bark and leaf extracts have been reported to have antioxidant, anticancer, anti-inflammatory, and antidiabetic properties. The plant has been used traditional medicine to treat a range of conditions, including diabetes, obesity, inflammatory conditions, dysentery, and even HIV.[13] A study found that the plant's leaf extract can eliminate reactive oxygen species, which can cause oxidative injuries.[13] The extract was also shown to have cytotoxic effects on human colon cancer cell line (HCT-116), but had little effect on normal cells. This suggests that *Swietenia mahagoni* could be a potential candidate for antitumor/cancer drugs.[13] However, no previous literatures have been recorded on HPLC phytochemical compounds profiling of ethanol *S. mahagoni* stem bark extract and their pharmacological importance in BPH management. Hence, the need for this study.

Materials and Methods

Plant collection and identification

The fresh stem bark of *Swietenia mahagoni* was harvested on September 2025, from Alege village, 6.633^0 N latitude and 9.15^0 E longitude, Obudu, LGA, Cross River State. The plant was identified and authenticated by taxonomist Dr Imoh Johnny of the Department of Plant Science (Botany), University of Uyo and voucher number: UUPH 49 © and was deposited the in the herbarium for future reference

Plant extraction

The bark of *S. mahagoni* was chopped into small pieces and air-dried for 3 weeks at room temperature. After which it was then pulverized with a 5.5HP Ginding Machine (model Gx 210, China). The 2 kg of the pulverized sample was dissolved in 3000 ml of 90% ethanol solution each and allowed for 72 hours. The samples was filtered with a cheesecloth and white man No 1 filter paper. The filtrate was then be concentrated with a rotatory evaporator (Bk-RE-1A) fitted to a 1 Stage vacuum pump (TW-1A, China) at 40 ^{0}C and store in the refrigerator till when it was ready for used.

HPLC Phytochemicals Screening

Procedure: A total of 10 g of the sample was measured into an amber bottle. To it, was added 20 ml of acetonitrile (acetonitrile/methanol), was added, shaken rigorously for 30 minutes. After the shaking, the aqueous end was run off with 25 ml of organic solvent and was collected into a standard flask, made up to the mark, and ready for the analysis.

Analysis

The standard from the (analytes) purple was first injected into the HPLC and this produced a chromatogram, with a given peak area and peak profile. These were used to create a window in the HPLC in preparation for the test sample analysis. Then, an aliquot of the extracted test sample was injected into the HPLC to obtain a chromatogram with corresponding peak profile and peak area. Then, the peak area of the sample was compared with that of the standard, relative to the concentration of the standard, to obtain the concentration of the sample.

We used the partial least square regression (PLS) to correlate HPLC fingerprints eith pharmacological activities of the identified compounds.

Results and Discussion

One of the main reasons men develop benign prostatic hyperplasia (BPH) is the conversion of testosterone to DHT by 5α-reductase type 2. In this study, 20 phytochemicals were identified from the HPLC screening stem bark crude extract of *S. mahagoni* as presenting in Table 1 and Figure 1. Research has shown that inhibiting this enzyme can be an effective way to manage the condition. Studies have used plant-based compounds to help alleviate BPH symptoms in rats, with promising results. Looking at our result, the compound called stigmasterol, found in plants, was detected and fits into a larger class called phytosterols. In a recent study by.[9], animals given stigmasterol orally for 21 days, significantly reduced DHT, prostatic size, and the activity of the enzyme by downregulation of prostatic 5α-reductase and AR expression, and decreased PCNA (a proliferation marker) at 100 mg/kg/day. It also causes programmed cell death apoptosis through upregulation of Bax and downregulation of Bcl-2, making it a promising single compound for BPH.[14, 15]

Another plant-based compound, beta-sitosterol, a phytosterol, has also been shown to be effective in alleviating BPH. It acts by reducing DHT level, and inflammation in the prostate, which can improve urine flow and reduce the need for frequent urination.[16] Studies have shown that beta-sitosterol is safe and effective in clinical trials, and can even outperform placebos in men.[17] In a recent study by [18] using a highly concentrated β-sitosterol formulation (APOPROSTAT® Forte), found that it could inhibit muscle contraction in the prostate and slow down the growth of prostate cells without causing any harm. This provide a clear explanation for why beta-sitosterol is so effective in improving urinary flow and reducing post-void residual urine volume improving urinary flow and reducing post-void residual volume in BPH patients.[18]

Based on.[19] reports, quercetin has been found to significantly lower PSA, DHT, and 5α-reductase activity in testosterone-induced BPH rats. When given to comparable models, kaempferol produced a notable decrease in the prostate index and improved histological changes. Additionally, it lowers mitochondrial ROS production in LPS-stimulated prostate organoids.[20,21] In male rats, epicatechin gallate, a flavonol, has also been demonstrated to reduce testosterone-induced prostatic hyperplasia by suppressing oxidative stress and 5α-reductase inhibition.[22]

A direct study on naturally occurring piperidine and a report has not been found, but synthetic piperidine-containing compounds such as piperine have been demonstrated to act as antioxidant, anticancer, anti-inflammatory, and antimicrobial properties.[23] It has also been shown to inhibit human 5α--reductase type 2 with nanomolar half-maximal inhibitory concentration (IC_{50}) values, and piperidine-based 17β-HSD type 5 antagonists have been patented for BPH as reported by.[24] Therefore, the piperidine framework might be beneficial for medicinal development.

Chronic inflammation, a hallmark of the condition, has been identified as a major factor advancing BPH, promoting fibrosis and increasing symptoms. Several compounds examined herein influence inflammation by additive mechanisms. Swietenine was recently investigated by.[25] another bioactive compound found in *S. mahagoni* stem bark extract. The presence of a tetranortriterpenoid has also been reported in *Swietenia macrophylla* seeds. In an in vitro study by Mak *et al*., found in an *in vitro* study employing LPS-stimulated RAW 264.7 macrophages, swietenine significantly reduced NO production and reduced IL-6, IL-1β, TNF-α, IFN-γ, COX-2, and NF-κB p65.[26] It also boosts the cell's antioxidant defence by activating the Nrf2 pathway, increasing Nrf2, HO-1, and NQO1 expression. Significantly, swietenine was found to be metabolically stable in mouse, rat, and human liver microsomes.[25] However, it has not been tested in BPH models yet, but these properties make it a highly promising candidate for the inflammatory component of BPH.

Swietenolide is a limonoid. In a recent diabetic study on mice with cognitive impairment revealed that swietenolide achieves anti-inflammatory effects through the activation of Nrf2 and subsequent suppression of the TXNIP/NLRP3 inflammasome.[26,27] Swietenolide acts by timulating increase level and boosting glutathione and superoxide dismutase while lowering malondialdehyde levels. The Nrf2–TXNIP–NLRP3 pathways are directly related to BPH because NLRP3 inflammasome activation has been detected in human hyperplastic prostates .[11, 27]

Flavonoids, Lucenin, rhamnetin and rutin have antioxidant properties in tests. Rhamnetin has been found to exhibit anti-inflammatory microglial cells and rat oedema and lowered miconazole-induced ROS and apoptosis in cardiomyocytes. Rutin and its derivatives have been studied primarily in the context of prostate cancer, focusing on AKT, EGFR, and ERK pathways. There are no direct BPH tests available for these compounds.[20, 21] Stigmasterol, as stated earlier, not only lowers

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DHT and AR but also directly causes apoptosis by lowering Bcl-2 and raising Bax, therefore lowering proliferation by lowering PCNA.[5] Among the natural products mix is uncommon.

This stem bark extract of *S. mahagoni* is a possible candidate for BPH management because it has anti-proliferation and pro-apoptotic properties.[5] Catechins and proanthocyanidins. Epicatechin gallate has demonstrated anti-hyperplastic effects in rats.[12] Proanthocyanidins, an oligomeric flavonoid, act as membrane androgen receptor agonists and cause apoptosis in hormone-independent prostate cancer cells; yet, no BPH-specific research has been published since 2020. An attractive idea, but still without direct BPH evidence, procyanidin B3 is a selective inhibitor of p300-mediated AR acetylation, a process that might regulate AR signalling in BPH without total blockage.[20,21]

Table 1: HPLC-Identified Phytochemical Constituents of *Swietenia mahagoni* Extract with Retention Time and Peak Parameters

Compound	Retention Time (min)	Area	Height	External	Units
Oxalic Acid	1.35	40.962	2.766	0.0000	%
Lucenin 2	2.016	77.811	9.065	7.7811	ppm
Swietenine	3.7	1779.615	46.217	0.0000	
Swietenolide	5.883	424.598	8.676	0.0000	
Swietmahonin E	6.966	41.155	3.957	0.0000	
Swietenitin	7.966	815.131	16.979	0.0000	
Catechin	9.116	64.485	3.566	0.0000	
Epicatechin	10.5	73.433	3.119	0.0000	
Scopoletin	11.3	46.662	2.417	0.0000	
Stigmasterol	11.85	41.09	1.639	0.0000	
Beta-Sitosterol	12.65	48.076	3.866	0.0000	ppm
Piperidine	13.833	54.877	3.748	5.4877	
Quercetin	15.5	630.014	12.485	0.0000	
Kaempferol	17.233	2312.239	34.783	0.0000	
Rutin	19.166	42.0325	3.25	0.0000	
Rhamnetin	19.95	42.841	5.715	0.0000	
Melionine	21.066	59.777	5.508	0.0000	
Germacrene D	21.983	92.031	6.543	0.0000	
Swietemacrophyllanin	23.083	46.41	4.298	0.0000	
Swietephragmin H	25.016	47.171	2.496	0.0000	

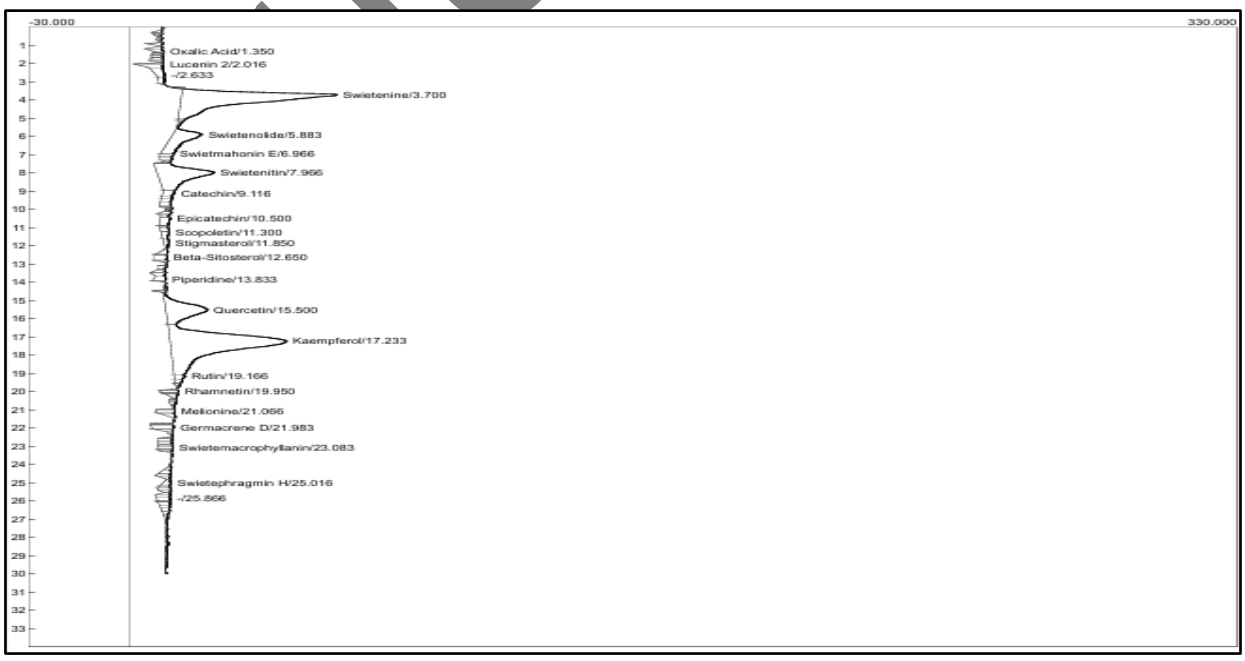

Figure 1: HPLC Chromatogram of *Swietenia mahagoni* Extract Showing Peaks Corresponding to Phytochemicals Listed in (Table 1)

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Conclusion

Out of the 20 phytocompounds we found, stigmasterol and β-sitosterol really stood out for treating BPH. They work by blocking an enzyme called 5α--reductase inhibition, lowering the activity of certain receptors, reducing inflammation, and flavonoids like epicatechin gallate, kaempferol, and quercetin have some promising effects but require an improve bioavailability. Limonoids like swietenine and swietenolide are promising candidates as anti-inflammatory and Nrf2-activating agents that might be effective in BPH management in animal studies. Compounds like lucenin, rhamnetin, and all other limonoids are yet to be reported as effective in BPH treatment. A strategy that uses multiple compounds and focuses on hormones, inflammation, and oxidative stress could be the best way to find natural treatment for BPH that could serve as a replacement for conventional drugs with notable side effects.

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Authors' Declaration

The authors hereby, declare that the work presented in this article are original and that any liability for claims relating to the content of this article will be borne by them.

Conflict of interest

The authors declare no conflict of interest.

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