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Exploring the Therapeutic Potential of Sphenocentrum jollyanum Root Extract in Malaria Treatment: Efficacy, Safety, and Future Directions

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ABSTRACT

Malaria remains a critical global health challenge, necessitating the exploration of novel therapeutic agents. This review examines the therapeutic potential of the ethanol root-extract of *Sphenocentrum jollyanum*, a plant traditionally used in West Africa for malaria treatment. Utilizing the Plasmodium berghei rodent model, which mirrors human malaria, we assess the extract's efficacy in restoring haematological markers, safety profile, and potential as an adjunct or alternative therapy. *Sphenocentrum jollyanum*, known for its rich phytochemical composition, including alkaloids, flavonoids, saponins, tannins, and terpenoids, has demonstrated significant restorative effects in preliminary studies. The extract improved hemoglobin levels, red blood cell counts, and platelet counts in infected mice, indicating potential benefits in mitigating malaria-induced anemia and other haematological abnormalities. Its mechanisms of action include antioxidant, anti-inflammatory, and immunomodulatory effects. Despite its promising results, rigorous safety evaluations are necessary, including acute and chronic toxicity studies, to ensure its safe use. Future research should focus on clinical trials to validate efficacy, optimize dosage, and explore combination therapies with standard antimalarial drugs. The review emphasizes the need for standardized preparation methods, quality control, and integration into public health strategies to enhance malaria management, particularly in resource-limited regions.

Keywords: Sphenocentrum jollyanum Root Extract, Malaria, Treatment, Efficacy, Safety.

INTRODUCTION

Plasmodium berghei, a rodent malaria parasite, is a key model for malaria research, providing insights into disease mechanisms closely related to human malaria. Its life cycle mirrors that of human-infecting Plasmodium species, making it a valuable tool for studying malaria's complex interactions [1]. This model allows for genetic manipulation, gene function study, pathogenesis development, and new treatment strategies. Sphenocentrum jollyanum, an indigenous plant in West Africa, has traditionally been used for its therapeutic properties, including malaria treatment. The root extract of this plant, known as "African yellow wood," has been used for fever, digestive disorders, and inflammation. Its pharmacological properties are attributed to its rich phytochemical composition, including alkaloids, flavonoids, saponins, tannins, and terpenoids. Ethanol extraction is a common method for obtaining these bioactive compounds. Recent studies have shown the potential of Sphenocentrum jollyanum root extract in restoring altered haematological markers in Plasmodium berghei-infected mice [2]. This review aims to explore the efficacy of this extract in malaria treatment, focusing on its restorative effects, safety profile, and potential as an adjunct or alternative therapy. Future research directions will also be discussed.

Traditional Uses and Pharmacological Properties of Sphenocentrum jollyanum

Sphenocentrum jollyanum, also known as "African yellow wood" or "Aduro oso" in some West African languages, is a plant native to various parts of West Africa, including Nigeria, Ghana, and Cameroon. It has a long history of use in traditional African medicine, with different parts of the plant, particularly the roots, being utilized for their therapeutic properties [3]. The plant's ethnobotanical significance lies in its purported health benefits, which are often passed down through generations. Preparation methods involve drying, grinding, or soaking the roots in

alcohol to prepare tinctures, which are then administered orally or topically. Sphenocentrum jollyanum has a wide range of medicinal properties due to its rich phytochemical composition. It is used for malaria treatment, digestive disorders, fever and pain relief, anti-inflammatory and antioxidant effects, and aphrodisiac effects. The pharmacological properties of Sphenocentrum jollyanum are largely attributed to its diverse array of bioactive compounds. Key phytochemicals include alkaloids, flavonoids, saponins, tannins, and terpenoids [4]. While traditional uses of Sphenocentrum jollyanum are well-documented, scientific research is ongoing to validate these claims and understand the mechanisms underlying its therapeutic effects. Sphenocentrum jollyanum is a significant medicinal plant in West African traditional medicine, revered for its wide range of therapeutic applications. Its rich phytochemical profile underlies its various medicinal properties, making it a valuable subject for further pharmacological research.

Preparation and Standardization of Ethanol Root-extract of Sphenocentrum jollyanum

The preparation and standardization of the ethanol root-extract of Sphenocentrum jollyanum involves several steps to ensure the extraction of active compounds in their most effective form. These steps include collection, identification, cleaning, drying, powdering, extraction, solvent selection, maceration, filtering, concentration, storage, and preservation [5]. Phytochemical profiling is crucial to ensure consistent levels of bioactive compounds in each batch of the extract. This can be done through qualitative analysis, quantitative analysis, calibration and validation, batch-to-batch consistency checks, adjustments, bioassays, physicochemical parameters, microbial and heavy metal testing, and storage stability studies. The collection and identification of the plant material are done by authenticating it by a botanist. The roots are thoroughly cleaned to remove contaminants, dried in a well-ventilated area, and ground into a fine powder. Ethanol is chosen as the solvent due to its effectiveness in extracting various phytochemicals. After maceration, the extracted extract is filtered using a rotary evaporator under reduced pressure to remove the ethanol, leaving behind a concentrated extract [6]. The concentrated extract is stored in airtight containers, preferably in a cool, dark place to prevent degradation of the active compounds. Standardization techniques such as calibration curves, method validation, batch-to-batch consistency checks, bioassays, moisture content, pH and solubility, microbial and heavy metal testing, and storage stability studies are used to ensure the safety and efficacy of the extract.

Experimental Design and Methodology

The efficacy of ethanol root-extract of Sphenocentrum jollyanum in restoring altered haematological markers in Plasmodium berghei-infected mice. Mice of similar age and weight are chosen for the study due to their well-documented immune responses and susceptibility to Plasmodium berghei infection. Protocol must be approved by an Institutional Animal Care and Use Committee (IACUC) or equivalent ethical review board to ensure humane treatment of animals [7]. Mice are housed in standard laboratory conditions with controlled temperature, humidity, and a 12-hour light/dark cycle. The experimental design includes animal selection, grouping, and administration methods. Preliminary studies determine the appropriate dosage range for the ethanol root-extract, while dose selection involves selecting multiple doses based on preliminary studies. Dosage preparation involves preparing the extract at desired concentrations and volume based on the body weight of each mouse. The methods for Plasmodium berghei infection, including parasite preparation, inoculation, and monitoring of infection progression. Blood samples from the tail vein of each mouse are collected at regular intervals to assess parasitemia. Automated methods are used to quantify parasitemia more efficiently. Clinical signs include health monitoring, body weight measurements, and haematological analysis [8]. Mortality is recorded to evaluate the impact of infection and treatment on survival, while survival curves are plotted to compare survival rates between different groups. A well-structured experimental design and robust methodology are critical for evaluating the efficacy of ethanol root-extract of Sphenocentrum jollyanum in restoring altered haematological markers in Plasmodium berghei-infected mice.

Assessment of Haematological Markers in Malaria

Malaria, caused by Plasmodium parasites, significantly alters haematological parameters, including hemoglobin levels, red blood cell count (RBC), white blood cell count (WBC), and platelet count. Hemoglobin levels are affected by the hemolysis of red blood cells (RBCs), which is crucial for oxygen transport and causes anemia. RBC count is typically measured in grams per deciliter (g/dL). Leukopenia or leukocytosis are caused by the immune system's response to infection, with specific changes depending on the infection's severity and stage. Platelet count is also affected by thrombocytopenia, a common complication of malaria [9]. Various techniques and instruments are employed to assess haematological markers in malaria-infected mice, including blood sample collection, hemoglobin measurement using the Cyanmethemoglobin Method, automated hematology analyzers, manual counting of RBCs under a microscope, manual differential counting of WBCs, and automated analyzers for platelet counts. Additional parameters include mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), and mean corpuscular hemoglobin concentration (MCHC). Quality control is ensured through regular calibration

of hematology analyzers and running control samples alongside experimental samples. The assessment of haematological markers is essential for studying malaria pathogenesis and evaluating the therapeutic efficacy of treatments like the ethanol root-extract of Sphenocentrum jollyanum [10]. By using precise methods for measuring hemoglobin levels, RBC count, WBC count, and platelet count, researchers can gain insights into the impact of malaria and the potential benefits of traditional medicinal plants in restoring normal haematological function.

Effects of Plasmodium berghei Infection on Haematological Markers

Plasmodium berghei infection in mice is a significant model for studying the haematological impacts of malaria [11]. Key changes observed include a reduction in hemoglobin levels due to the hemolysis of infected red blood cells (RBCs), leading to anemia, pallor, lethargy, and weakness. The parasite also causes a significant drop in red blood cell count, exacerbated by the reduction in RBC count. White blood cell counts (WBC) are often observed in the early stages of infection, reflecting the initial immune suppression or redistribution of white blood cells to infection sites. As the infection progresses, leukocytosis can occur, indicating an immune response to the parasite, typically seen in neutrophils. Platelet count decreases significantly in Plasmodium berghei-infected mice, increasing the risk of bleeding and hemorrhagic complications [12]. These changes closely mirror those seen in human malaria patients, providing valuable insights into the pathophysiology of the disease. Infected mice exhibit significant anemia due to hemolysis of RBCs, while human malaria patients experience hemolytic anemia, a hallmark of malaria, particularly in Plasmodium falciparum infections. Additional markers observed in infected mice include changes in mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), and mean corpuscular hemoglobin concentration (MCHC), reflecting the impact of the infection on RBC size and hemoglobin content. Elevated levels of lactate dehydrogenase (LDH) and bilirubin are common, indicating hemolysis and liver involvement. The haematological alterations induced by Plasmodium berghei infection in mice provide a valuable model for understanding the pathophysiology of malaria and its impact on blood parameters. Understanding these changes helps in diagnosing, monitoring, and treating malaria, contributing to improved clinical outcomes.

Restorative Effects of Ethanol Root-extract of Sphenocentrum jollyanum

The ethanol root-extract of Sphenocentrum jollyanum has been found to have restorative effects on altered haematological markers in Plasmodium berghei-infected mice. The extract contains bioactive compounds with antioxidant and anti-inflammatory properties, which may help protect red blood cells from the parasite's hemolytic effects. Mice treated with the extract showed a significant increase in hemoglobin levels compared to untreated controls, suggesting that the extract mitigates the hemolytic effects of the parasite [13]. The extract may promote erythropoiesis, the production of new red blood cells, and reduce the destruction of existing red blood cells. The extract-treated group showed a more balanced white blood cell count compared to untreated infected mice, suggesting an improvement in immune system regulation. Additionally, the extract may contain compounds that support platelet production or prevent their excessive consumption and destruction. Comparatively, standard antimalarial treatments, such as chloroquine and artemisinin-based combination therapies, are highly effective in reducing parasitemia and alleviating malaria symptoms. However, the ethanol root-extract of Sphenocentrum jollyanum's restorative effects on haematological markers provide a complementary benefit, potentially enhancing recovery and reducing complications.

Mechanisms of Action

The ethanol root-extract of Sphenocentrum jollyanum is believed to have therapeutic effects through various mechanisms, including immunomodulation, antioxidant activity, and other pharmacological actions [14]. These mechanisms include the enhancement of the immune system's ability to combat infections, regulation of inflammation, reduction of oxidative stress, enhancement of antioxidant enzymes, inhibition of inflammatory pathways, protection against cell damage, stimulation of erythropoiesis, preservation of platelet function, and direct anti-parasitic effects. Immunomodulatory properties involve activating immune cells and regulating cytokine levels, promoting a more effective and controlled immune response. Antioxidant properties involve free radical scavenging, preventing oxidative damage, and reducing inflammation markers. Anti-inflammatory properties support the repair and regeneration of tissues affected by the infection, while hematoprotective actions support red blood cell production and maintaining platelet function. Additional properties include liver protection, which can enhance overall recovery and reduce liver-related complications. The extract may also exhibit broader antimicrobial activity, contributing to overall health and infection resistance. The ethanol root-extract of Sphenocentrum jollyanum demonstrates a multifaceted mechanism of action, including immunomodulation, antioxidant activity, anti-inflammatory effects, and hematoprotective actions. Understanding these mechanisms helps elucidate the potential benefits of the extract as a complementary therapy in malaria management [15].

Toxicological and Safety Assessment

The toxicological and safety assessment of the ethanol root-extract of Sphenocentrum jollyanum involves a comprehensive evaluation of acute and chronic toxicity. Traditional use suggests a relatively safe profile, but scientific validation is essential to confirm safety and efficacy in modern contexts. The ethanol root-extract's composition helps identify potential toxic compounds and ensures only beneficial phytochemicals are present at safe levels [16]. Acute toxicity studies aim to determine the immediate harmful effects of the extract following a single dose or short-term exposure, establishing a safe dose range. These studies are conducted using animal models, such as mice or rats, and endpoints include mortality rates, behavioral changes, signs of distress, and physical symptoms. If the extract is found to have low toxicity, it will indicate a high dose tolerance with minimal adverse effects. Chronic toxicity studies assess the long-term effects of repeated exposure to the extract over an extended period, determining the safety of the extract for prolonged use. The safety profile is often evaluated by administering the extract at various doses to establish a safe and effective range. Safety margins are calculated to ensure that the effective therapeutic dose is well below the level at which adverse effects occur, providing a buffer to prevent toxicity in human applications. The extract's safety profile must comply with regulatory guidelines and standards for herbal products and dietary supplements.

Implications for Malaria Treatment

The ethanol root-extract of Sphenocentrum jollyanum holds significant potential as an adjunct and alternative therapy for malaria treatment. Its ability to restore haematological markers and its potential anti-parasitic effects could enhance overall recovery and improve patient outcomes when used in conjunction with drugs like chloroquine or artemisinin-based combination therapies (ACTs). Combining the extract with standard treatments might reduce side effects associated with conventional antimalarials, such as gastrointestinal disturbances or neurotoxicity. Herbal medicine is another potential therapy option, especially in regions where conventional antimalarials are less accessible or face resistance issues [17]. If the extract demonstrates direct anti-parasitic activity, it could contribute to combating malaria resistance by providing an alternative or supplementary approach to current antimalarial drugs. Access and affordability could also be improved in resource-limited settings. Future research directions include clinical trials, combination studies, mechanistic studies, standardization and quality control, long-term safety studies, drug interaction studies, and accessibility and implementation. Phase I and II trials will evaluate the safety, efficacy, and optimal dosing of the ethanol root-extract in humans, while long-term safety studies will assess the safety of prolonged use of the extract in diverse populations and under varying health conditions. Public health integration will assess the potential for integrating the extract into national malaria control programs and public health initiatives to improve malaria management and outcomes.

CONCLUSION

The ethanol root-extract of Sphenocentrum jollyanum has shown significant restorative effects on haematological markers in Plasmodium berghei-infected mice, increasing hemoglobin levels, red blood cell count, and platelet count while normalizing white blood cell count. Its therapeutic effects are likely due to its immunomodulatory, antioxidant, and anti-inflammatory properties, which help reduce oxidative stress, modulate immune responses, and improve overall hematological health. To confirm its long-term safety and potential drug interactions, further research is needed. Clinical trials should be conducted to evaluate the safety, efficacy, and optimal dosage of the ethanol root-extract in humans. Combination therapy trials should be investigated to assess synergistic effects and optimize treatment regimens. Mechanistic research should involve detailed mechanism exploration, phytochemical profiling, standardization and quality control, regulatory compliance, long-term safety studies, and community acceptance. Standardization and quality control methods should be established to ensure consistent quality and potency of the extract. Long-term safety studies should evaluate the effects of prolonged use of the extract, especially in diverse populations and under varying health conditions. Production and distribution methods should be explored for large-scale production and distribution, particularly in malaria-endemic regions. Public health integration strategies should be assessed to enhance malaria management and treatment outcomes. Cultural and socioethical considerations should be considered to design effective health education and promotion strategies.

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