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Exploration of Phytochemical Composition and Anticancer Potential of Commiphora wightii Stem Bark

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Abstract

This comprehensive research delves into the intricate world of Commiphora wightii, a botanical marvel native to the arid and semi-arid landscapes of northern India. The primary focus is on unraveling the phytochemical intricacies and exploring the potential anticancer properties residing in the stem bark of this resilient shrub. The study employs a multifaceted approach, involving the isolation and characterization of sulforhodamine B (SRB) and guggulsteronefrom the plant's oleogum resin. Beyond mere chemical analysis, the investigation spans historical, economic, and practical dimensions, providing a holistic understanding of the plant's role in traditional Ayurvedic practices and its contemporary applications.

Key word : Anti-cancer , Commiphora wightii , sulforhodamine

Introduction

Commiphora wightii, belonging to the Burseraceae family, stands as a testament to the rich biodiversity of India, thriving in regions such as Rajasthan, Karnataka, and Gujarat. Its distinctive features, embodied in a resilient

stature of 4 to 6 feet and a telltale thin papery bark, have not only made it a botanical spectacle but also earned it a revered place in Ayurveda. [1] The oleogum resin, fondly referred to as Guggulu, takes center stage in this exploration, with a detailed examination of its five distinct types, notably Krishnan (black) and Peet varn (yellow), recognized for their consumable suitability. [2]

Fig 1a: Commiphora wightii Plant

Fig 1b: oleogum resin of C.wightii

Historical Significance and Economic Utility

The roots of Commiphora wightii's significance stretch deep into history, finding mention in ancient scriptures like the Atharvaveda and gaining elaboration in the Chikitsa Sthanam of Charaka Samhita. This historical context weaves a narrative of the plant's traditional applications in holistic medicine, providing a cultural backdrop to its contemporary relevance. [3] Economically, the spotlight falls on the oleogum resin, a pivotal component exuded by specialized cells in the stem-bark. The resin, with its nuanced composition of 6.9% moisture, 0.6% volatile oil, 61% resin, 29.6% gum, and 3.2% insoluble substances, emerges not merely as a biological secretion but as a valuable resource with multifarious applications. [4,5]

Harvesting and Characteristics

The process of harnessing the resin involves the intricate artistry of the natives, who carefully incise the bark, coaxing forth a yellowish oleoresin. This substance undergoes a fascinating metamorphosis upon exposure to air—drying, hardening, and acquiring a reddish-brown hue. The economically viable part of the plant, the oleogum resin, becomes the focal point of economic and medicinal endeavors. Its characteristics, from the golden type and semi-solid consistency in its fresh state to the transformation into a yellow-brown color after solidification, contribute to its market value. A characteristic aromatic scent and a bitter, astringent taste complete the sensory profile of this botanical treasure. [6,7,8]

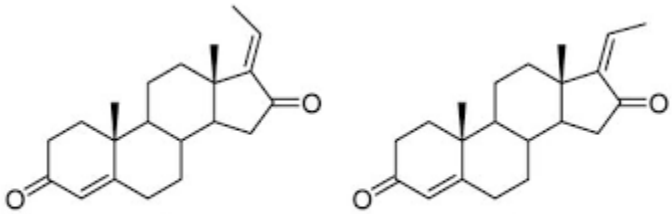
Modern Dietary Supplements and Applications

The journey of Commiphora wightii transcends ancient scripts and finds itself embedded in the fabric of modern dietary supplements. The raw material, revered in Indian medicine, takes diverse forms, from capsules to powders. Its integration into formulations such as Gokshurandiguggulu for urinary tract diseases, Kaishorguggulu for skin ailments, and Mahayogarajaguggulu for gout and rheumatism exemplifies its versatility. Beyond the Indian market, Guggulu finds its way to European herbal and health food stores and pharmacies, attesting to its global recognition. [9]

Fig 2**:** Modern Dietary Supplements of Commiphora wightii's

Medicinal Properties and Active Compounds

Commiphora wightii's journey in the realm of medicinal exploration takes a pivotal turn with the revelation of its potent hypolipidemic agent, the guggul lipid. The ethyl acetate extract of C. wightii emerges as a protagonist in the narrative, showcasing significant in vitro cytotoxicity. The subsequent isolation of compounds, including Guggulsterone (Z-Guggulsterone, E-Guggulsterone) [10] and a novel class of naturally occurring lipids, adds layers to the plant's pharmacological profile.

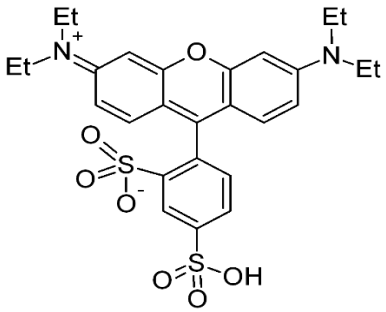


1a ***E*-Guggulsterone** **1b** ***Z*-Guggulsterone**

Isolation of Sulforhodamine B (SRB)

The scientific endeavor takes a fascinating turn as the researchers embark on isolating Sulforhodamine B (SRB) from the powdered bark of Commiphora wightii. This involves a meticulous process of grinding the bark into a fine powder, followed by a judicious selection of solvents like methanol or ethanol for extraction. The resulting solution undergoes a series of filtrations and, if necessary, concentration methods such as rotary evaporation. The final solution is subjected to rigorous analysis using UV-Visible spectrophotometry, ensuring a detailed understanding of SRB's presence and concentration. [7]

Molecular formula =$C_{27}H_{30}N_2O_7S_2$



Chemical Structure of Sulforhodamine B (SRB)

Inhibition of NF-κB Activity [11, 12,]

Commiphora wightii, commonly known as guggul, has demonstrated profound inhibitory effects on the activity of nuclear factor-kappa B (NF-κB). NF-κB is a pivotal transcription factor known for its regulatory role in numerous cellular processes, including inflammation, immune response, and cell survival. The modulation of NF-κB activity is of significant interest in the context of various diseases, especially cancer, where aberrant NF-κB signaling is often implicated.

In the luciferase reporter assay conducted in the current study, various samples were subjected to scrutiny, including the guggul extract (GU-M), different fractions, and isolated compounds. All these samples were meticulously dissolved in dimethyl sulfoxide (DMSO), stored at -20°C, and subsequently utilized for biological screening.

The experimental platform involved the use of 4T1 cells stably expressing luciferase with an NF-κB/Luc2 reporter gene, specifically designated as 4T1-NFκB-Luc2 cells. This model system was paramount for examining NF-κB-dependent transcriptional activity. The cells were carefully seeded in a 96-well plate, allowing for adherence and incubated for 24 hours to establish a robust cellular milieu.

Following the incubation period, the cells were subjected to various treatments, which included the application of the indicated sample extracts, fractions, isolated compounds, or the vehicle control (DMSO) for specified durations. This meticulous design aimed to capture the dynamic response of NF-κB signaling to the diverse components present in the guggul extract.

As a final step in the luciferase reporter assay, D-luciferin, a substrate for the luciferase enzyme, was introduced to each well. The subsequent luminescence emitted from the cells was then measured using an in vivo imaging system, providing a quantitative readout of NF-κB-dependent transcriptional activity.

Parallelly, the study incorporated an assessment of cell viability using the CCK-8 reagent, a widely utilized tool for evaluating cellular metabolic activity and proliferation. This involved measuring absorbance at specific wavelengths with an absorbance plate reader.

The utilization of this multifaceted approach allowed for a comprehensive evaluation of the impact of Commiphora wightii and its constituents on NF-κB signaling, shedding light on the potential mechanisms underlying the observed effects. The detailed analysis of transcriptional activity and its correlation with cell viability provided valuable insights into the dynamic interplay between guggul components and NF-κB-mediated cellular responses.

The findings from this luciferase reporter assay align with a broader context in which researchers seek potent inhibitors of NF-κB activity. The NF-κB pathway, with its intricate network of signaling cascades, is a central player in orchestrating cellular responses to external stimuli. In the context of cancer, dysregulation of NF-κB is frequently associated with uncontrolled cell proliferation, resistance to apoptosis, and promotion of an inflammatory microenvironment conducive to tumor progression.

Commiphora wightii's ability to modulate NF-κB activity underscores its potential as a valuable resource in the development of anti-cancer therapeutics. The nuanced understanding gained from this study positions guggul and its derivatives as promising candidates for further exploration in the realm of cancer research. The multifaceted approach adopted in this investigation, combining molecular assays with viability assessments, adds depth to the comprehension of the intricate interplay between guggul components and NF-κB signaling. As research advances, these insights may pave the way for the development of novel therapeutic strategies targeting NF-κB dysregulation in various diseases, particularly cancer.

Anti-Apoptotic Proteins and Cancer Protection [13,14]

Commiphora wightii emerges as a botanical protagonist in the realm of cancer protection, showcasing a remarkable ability to modulate the levels of anti-apoptotic proteins. These proteins, belonging to the B-cell lymphoma (Bcl) family, play a pivotal role in cellular survival by inhibiting the process of apoptosis, a mechanism that naturally regulates cell death. The intricate dance between Commiphora wightii and these anti-apoptotic proteins unfolds as a compelling narrative in the pursuit of understanding and harnessing its potential in cancer prevention.

Among the key players in the Bcl family is Bcl-2, an anti-apoptotic protein renowned for its capacity to enhance cell survival. Elevated expression of Bcl-2, when coupled with factors promoting cytotoxic tendencies, becomes a precursor to cancer development. Commiphora wightii, through its active component guggulsterone, intricately orchestrates a reduction in Bcl-2 levels, thereby disrupting the delicate balance that sustains prolonged cell survival.

A parallel protagonist in this narrative is Bcl-XL, a protein intricately involved in cellular migration and mitochondrial metabolism across various human cell types. Increased expression of Bcl-XL is not merely an innocent bystander; it has the potential to contribute to carcinogenesis. In a meticulous study involving human prostate cancer cells, the application of guggulsterone from Commiphora wightii resulted in a discernible reduction in both Bcl-2 and Bcl-XL levels. This reduction, occurring after 16-24 hours of treatment, points towards the dynamic and time-sensitive nature of Commiphora wightii's influence on these critical anti-apoptotic players.

Commiphora wightii, acting as a botanical guardian against carcinogenesis, extends its influence beyond the realms of Bcl-2 and Bcl-XL. Another noteworthy actor in this saga is Bcl-W, a protein sharing structural and functional similarities with Bcl-XL. Elevated levels of Bcl-W are known to impede cellular death under cytotoxic conditions, contributing to the pro-survival landscape within cells. Commiphora wightii, particularly through its constituent guggulsterone, exerts its anti-cancer effects by orchestrating the downregulation of Bcl-W. This strategic move, akin to the flick of a molecular switch, induces apoptosis in cancer cells, further cementing Commiphora wightii's role as a guardian against unchecked cellular proliferation.

In the intricate choreography of cancer protection, Mcl-1 takes center stage as an anti-apoptotic protein with profound implications for cellular survival. Commiphora wightii, armed with its active components, including terpenoids and guggulsterone, navigates the complex pathways within cells to reduce the levels of Mcl-1. Mcl-1's interference with cellular pathways, particularly its role in suppressing cytochrome c release from mitochondria, makes its downregulation a key strategy in promoting apoptosis. The delicate balance between Mcl-1 expression and cellular fate is thus tipped towards programmed cell death, a desirable outcome in the context of cancer prevention. [15]

The concluding act in this narrative introduces A1, an anti-apoptotic protein wielding influence over cell survival by acting on mitogen-activated protein. A1's overexpression has been implicated in various malignancies, including acute myeloid leukemia, melanoma, and lymphoma. Commiphora wightii, with its guggulsterone component, once again takes the stage as a modulator, downregulating the expression of A1 in tumor cells, including those implicated in oral and liver cancers. This orchestrated reduction in A1 levels aligns with Commiphora wightii's broader mission: to curtail the pro-survival mechanisms that underpin cancer progression. [16]

In essence, Commiphora wightii's influence on anti-apoptotic proteins paints a vivid portrait of a botanical ally in the fight against cancer. It’s strategic downregulation of Bcl-2, Bcl-XL, Bcl-W, Mcl-1, and A1 underscores a multi-pronged approach to disrupting the intricate ballet of cellular survival. As research unfolds, Commiphora wightii stands not just as a botanical specimen but as a potential source of inspiration for innovative therapeutic strategies in the ever-evolving landscape of cancer research and treatment. [17,18]

Conclusion:

In the expansive tapestry of botanical exploration, Commiphora wightii emerges as a multifaceted protagonist, weaving together threads of traditional medicine, economic utility, and, most notably, a potential ally in the battle against cancer. As this botanical saga unfolds, the intricate interplay between Commiphora wightii and its active components, particularly guggulsterone, unveils a compelling story of anti-apoptotic protein modulation and cancer protection.

The journey begins with the meticulous documentation of Commiphora wightii's botanical and historical significance. Rooted in the arid and semi-arid landscapes of northern India, this resilient shrub or small tree, adorned with thin papery bark, has entrenched itself in the annals of Ayurveda. Its oleogum resin, aptly named Guggulu, takes center stage, classified into five distinct types, with Krishnan (black) and Peet varn (yellow) standing out for their recognized suitability for human consumption.

Historical echoes resonate in ancient texts like the Atharvaveda, enriching the traditional roles of Guggulu in holistic medicine. Economically, the focus pivots to the oleogum resin, a vital substance secreted by specialized cells in the stem-bark. Comprising moisture, volatile oil, resin, gum, and insoluble substances, this resin becomes a valuable resource with diverse applications, mirroring the intricate interplay between botanical characteristics and economic utility.

The narrative gains momentum as Commiphora wightii traverses landscapes, finding itself not only in the realms of Ayurveda but also as a key player in contemporary dietary supplements. Its presence, particularly in Indian medicine, manifests in various formulations targeting diverse ailments. Guggul extract, available in capsule and powder form, becomes a sought-after agent for the prevention and treatment of diseases. Its availability in the European market, including Poland, underscores its global relevance and acceptance.

As the spotlight shifts to the isolation process, Commiphora wightii's stem bark becomes a source of Sulforhodamine B (SRB), a compound with implications for cancer research. The extraction journey involves meticulous steps, from powder preparation to solvent selection, stirring, filtration, and analysis. Safety measures echo throughout this process, emphasizing the need for tailored extraction procedures to ensure optimal results.

Delving deeper into the realm of pharmacology, Commiphora wightii's active component, guggul lipid, takes center stage as a potent hypolipidemic agent. Research ventures into the realm of cytotoxicity, uncovering the presence of ferrulates and a novel class of naturally occurring lipids with robust cytotoxic and free radical scavenging activity. The oleogum resin, a treasure trove of compounds, reveals a spectrum of pharmacological activities, further underscoring Commiphora wightii's significance.

The narrative takes an intriguing turn as the inhibitory effects of the oleogum resin on nitric oxide (NO) production come to the forefront. Through luciferase reporter assays, guggul extract, fractions, and isolated compounds stand as protagonists, showcasing their influence on NF-κB-dependent transcriptional activity. The study, driven by the quest for potent NF-κB inhibitors, unveils myrrh-triterpenes as formidable players, significantly inhibiting NF-κB activation and metastatic potential in triple-negative breast cancer cells.

The tale crescendos as Commiphora wightii positions itself as a guardian against cancer development. Its nuanced dance with anti-apoptotic proteins, from the downregulation of Bcl-2 and Bcl-XL to the strategic modulation of Bcl-W, Mcl-1, and A1, unfolds as a symphony of orchestrated cellular responses. The reduction in these pro-survival proteins aligns with the broader mission of inducing apoptosis in cancer cells, presenting Commiphora wightii as a potential beacon in the ever-expanding landscape of cancer research and therapeutic interventions.

In conclusion, Commiphora wightii's journey transcends geographical landscapes and historical epochs, resonating as a botanical protagonist with the potential to contribute significantly to our understanding of cancer prevention and treatment. As the chapters of research unfold, Commiphora wightii beckons researchers and

clinicians alike to delve deeper into its intricate nuances, offering a promising avenue for innovative therapeutic strategies in the ongoing battle against cancer.

his study suggested that Guggulsterone has apoptotic effects against various cancer types. Further investigation of its pharmacological activity and mechanism of action should be conducted. In vivo experiments and clinical trials are required to confirm the anticancer activity.

1. *The Ayurvedic Pharmacopoeia of India (Formulations)*, Department of Indian Systems of Medicine and Homeopathy, Ministry of Health and Family Welfare, Government of India, New Delhi, India, 1st edition, 2007.
2. *The Ayurvedic Pharmacopoeia of India*, Department of Indian Systems of Medicine and Homeopathy, Ministry of Health and Family Welfare, Government of India, New Delhi, India, 1st edition, 2001.
3. Sarup, P., Bala, S., & Kamboj, S. (2015). Pharmacology and Phytochemistry of Oleo-Gum Resin of Commiphora wightii (Guggulu). Scientifica, 2015, Article ID 138039. http://dx.doi.org/10.1155/2015/138039
4. N. L. Urizar and D. D. Moore, "Gugulipid: a natural cholesterol-lowering agent," *Annual Review of Nutrition*, vol. 23, pp. 303–313, 2003.
   View at: Publisher Site | Google Scholar
5. *Indian Pharmacopoeia*, The Controller of Publications, New Delhi, India, 1996.
6. The Ayurvedic Pharmacopoeia of India (Formulations) 1st. New Delhi, India: Department of Indian Systems of Medicine and Homeopathy, Ministry of Health and Family Welfare, Government of India 2007.
7. Zhu N, Rafi MM, DiPaola RS, Xin J, Chin C-K, Badmaev V, Ghai G, Rosen RT, Ho C-T. (2001) Bioactive constituents from gum guggul (Commiphora wightii). Phytochemistry 56, 723–727.
8. Siddiqui MZ. Guggul: An excellent herbal panacea. Asian J Pharm Health Sci. 2011; 1(1): 35–39.
9. Bessou M, Lopez J, Gadet R, Deygas M, Popgeorgiev N, Poncet D, et al. The apoptosis inhibitor Bcl-xL controls breast cancer cell migration through mitochondria-dependent reactive oxygen species production. Oncogene. 2020;39(15):3056–74. https://doi.org/10.1038/s41388-020-1212-9
10. Singh SV, Zeng Y, Xiao D, Vogel VG, Nelson JB, Dhir R, et al. Caspase-dependent apoptosis induction by guggulsterone, a constituent of Ayurvedic medicinal plant Commiphora mukul, in PC-3 human prostate cancer cells is mediated by Bax and Bak. Mol Cancer Ther. 2005;4(11):1747–54. https://doi.org/10.1158/1535-7163.mct-05-0223
11. Nardone G, Rocco A, Vaira D, Staibano S, Budillon A, Tatangelo F, et al. Expression of COX-2, mPGE-synthase1, MDR-1 (P-gp), and Bcl-xL: a molecular pathway of H pylori-related gastric carcinogenesis. J Pathol. 2004;202(3):305–12. https://doi.org/10.1002/path.1512
12. Hartman ML, Czyz M. BCL-w: apoptotic and non-apoptotic role in health and disease. Cell Death Dis. 2020;11(4):1–16.
13. Abu-Izneid T, Rauf A, Shariati MA, Khalil AA, Imran M, Rebezov M, et al. Sesquiterpenes and their derivatives-natural anticancer compounds: An update. Pharmacol Res. 2020;161:105165. https://doi.org/10.1016/j.phrs.2020.105165

14. Twilley D, Lall N. The role of natural products from plants in the development of anticancer agents. Nat Prod Drug Discov: Elsevier. 2018:139–78. https://doi.org/10.1016/B978-0-08-102081-4.00007-1

15. Bittker JA, Weiwer M, Wei G, Germain A, Brown E, Dandapani S, et al. Discovery of inhibitors of anti-apoptotic protein A1. Probe reports from the NIH MLP [Internet]. 2011. Available from: https://www.ncbi.nlm.nih.gov/books/NBK98916/

16. Shishodia S, Harikumar KB, Dass S, Ramawat KG, Aggarwal BB. The guggul for chronic diseases: ancient medicine, modern targets. Anticancer Res. 2008;28(6A):3647–64.

17. Abdellatef, A. A., Meselhy, M. R., El-Askary, H. I., El-mekkawy, S., & Hayakawa, Y. (Year). Anti-metastatic function of triterpene phytochemicals from guggul by targeting tumor-intrinsic NF-kB activation in triple-negative breast cancer cells. Phytomedicine Plus, Volume (Issue), Page range. https://doi.org/10.1016/j.phyplu.2022.100345.

18. Abdellatef, A. A., Zhou, Y., Yamada, A., Elmekkawy, S. A., Kohyama, A., Yokoyama, S., Meselhy, M. R., Matsuya, Y., Sakuraib, H., & Hayakawa, Y. (Year). Synthetic E-guggulsterone derivative GSD-1 inhibits NF-κB signaling and suppresses the metastatic potential of breast cancer cells. Biomedicine & Pharmacotherapy, Volume (Issue), Article ID, Page range. https://doi.org/10.1016/j.biopha.2021.111737