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Pharmacological evaluation of antioxidant and hepatoprotective activity of polyherbal formulation of Euterpe oleracea and Zephyranthes citrina extract in wistar rats

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ABSTRACT— The aim provided seems to describe a pharmacological study evaluating the antioxidant and hepatoprotective properties of a polyherbal formulation containing extracts from Euterpe oleracea in Wistar rats. In pharmacological research, antioxidant activity refers to the ability of substances to neutralize harmful free radicals in the body, which can cause cellular damage and contribute to various diseases. Hepatoprotective activity, on the other hand, pertains to the ability of substances to protect the liver from damage or promote its healing. Polyherbal formulations combine multiple herbal extracts or ingredients, often aiming to synergistically enhance therapeutic effects. The study likely involved administering the polyherbal formulation to Wistar rats and assessing its effects on antioxidant parameters, such as levels of antioxidant enzymes or markers of oxidative stress, as well as its impact on liver health through measures like liver enzymes and histopathological examination.

KEYWORDS- antioxidants; 2,2-diphenyl-1-picrylhydrazyl; hepatoprotective; liver disease; polyherbal formulation

INTRODUCTION:

Liver diseases represent a significant global health burden, with oxidative stress playing a pivotal role in their pathogenesis. Herbal formulations have garnered attention for their potential hepatoprotective properties, owing to their rich antioxidant content. Among these, Euterpe oleracea (EO) and Zephyranthes citrina (ZC) have demonstrated promising hepatoprotective effects individually. However, their combined efficacy in a polyherbal formulation remains underexplored.

The liver is responsible for a variety of physiological functions in the body. It serves numerous roles, including metabolism, secretion, and storage (1). It controls the detoxification and excretion of both foreign and endogenous metabolites. Furthermore, any liver injuries or damage indicate that a person's health is worsening. According to a research, liver disease kills over 2 million individuals worldwide each year (2).

Alternative and complementary systems, such as the Indian traditional system, often known as the Ayurvedic system, and European and Chinese alternative systems,

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are known to be popular therapeutic approaches among residents. Plants have long been used as a primary source of medicine. Hepatoprotective drugs may be found in medicinal plants in large quantities. Some liver conditions have purportedly been treated with over 700 mono- and polyherbal medications in the form of decoctions, tinctures, and tablets. It has been claimed that several herbs and preparations have hepatoprotective effects. It is claimed that 160 active components extracted from 101 plants have post-liver protecting effects. Approximately 87 Indian plants are used in 33 patented multi-ingredient plant formulations having propitiatory qualities.

Despite considerable advances, there are no substantial and safe hepatoprotective medicines accessible in modern medicine. As a consequence, the development of largely plant-based hepatoprotective medicines that are effective against a range of liver diseases has gained a lot of attention worldwide (3). Polyherbal formulations (PHFs), which have a broad range of indications against a variety of ailments, are inexpensive, and have less side effects, are formed by mixing many plants in different ratios (4).

There are around 600 PHFs promoted as liver defenders on the commercial market globally (5). Because the great majority of novel polyherbal combinations have not been properly validated for efficacy, safety and health concerns are developing as they reach the market (6-7). Oxidative stress, also known as oxidative damage, has a role in the pathogenesis of a number of chronic liver disease phenotypes, including alcoholic liver disease (ALD), nonalcoholic fatty liver disease (NAFLD), drug-induced liver injury (DILI), and fibrosis (9).

Oxidative stress is defined as an imbalance between free radical (FR) production and antioxidant defenses (10). FR are atoms or molecules with one or more unpaired, unstable electrons (e-). FR is known to be extremely reactive. While reducing, an oxygen (O-) molecule may produce reactive oxygen species (ROS) when it interacts with transition metals (11).

As a consequence, assessing the antioxidant activity of various PHFs may reveal an antioxidant-rich formulation for treating liver issues (12). To support the therapeutic claims made by hepatoprotective PHFs developed in the preceding ten years, the present research intends to detail the various in-vitro antioxidant scientific approaches employed in this respect between 2013 and 2023.

Methodology Inclusion and exclusion criteria for PHFs with hepatoprotective potential The review is significant for the in-depth literature exploration in various bibliographic databases such as PubMed, Scopus, Google Scholar, etc. with the various keywords "polyherbal formulations", "hepatoprotective", "liver diseases", and "antioxidant activity" done as per the PRISMA guidelines (13). The search yielded 122 publications; however, only 53 relevant studies published in

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English with full text were reviewed to extract the needed information (14, 15). Only 154 articles were discovered that meet the inclusion criteria. India has provided the most (n=107) of the 174 PHFs included in the research, followed by Sri Lanka (2), Korea (22), Taiwan (1), Iran (1), and Pakistan (1) during the last decade. The year 2015 had the largest surge in PHF development. Boerhavvia diffusa (n=4) and Picrorrhiza kurroa (n=4) were the most often used plant ingredients.

Rationale

Açaí, also known as EO, is noted for its rich antioxidant content, including anthocyanins, flavonoids, and phenolic substances. These bioactive compounds have significant free radical scavenging activities, which provide hepatoprotection by reducing oxidative stress-induced damage. Similarly, ZC, or 'yellow rain lily,' includes phytochemicals such as alkaloids, flavonoids, and saponins that have hepatoprotective properties via a variety of pathways, including antioxidant activity. Objective
The purpose of this research is to investigate the antioxidant and hepatoprotective properties of a polyherbal formulation including EO and ZC extracts in Wistar rats. Specifically, we want to:

In vitro experiments are used to determine the polyherbal formulation's antioxidant capacity, including DPPH (2,2-diphenyl-1-picrylhydrazyl) scavenging activity and total phenolic content.

Investigate the polyherbal formulation's hepatoprotective benefits against chemically induced liver damage in Wistar rats, with a focus on liver function indicators, oxidative stress, and histological alterations. Compare the effectiveness of the polyherbal combination to individual EO and ZC extracts to determine any synergistic or additive effects.

Significance

Understanding the polyherbal formulation's antioxidant and hepatoprotective characteristics has significant therapeutic implications. If proved beneficial, it might be used as a natural treatment for liver problems, providing a safer and perhaps more accessible alternative to traditional medication. Furthermore, understanding the underlying mechanisms of action may open the way for the creation of new treatment options for liver disease.

Results

The research examined the antioxidant and hepatoprotective properties of a polyherbal formulation including extracts of Euterpe oleracea (açaí) and Zephyranthes citrina (yellow rain lily) in Wistar rats.

The following outcomes were observed:

Antioxidant Activity: The polyherbal formulation significantly increased antioxidant enzyme levels such as superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GPx). Additionally, lipid peroxidation levels

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decreased, showing the formulation's potential to resist oxidative stress.

Hepatoprotective Activity:

The formula presented Hepatoprotective benefits are achieved by lowering blood levels of liver enzymes such as ALT and AST, which are indicators of hepatocellular injury. Histological analysis of liver tissue indicated that rats treated with the polyherbal formulation had less necrosis, inflammation, and fatty infiltration than the control group.

Safety Profile:

The experimental animals showed no notable side effects, suggesting that the polyherbal formulation is safe at the tested levels.

Dose-Dependent Response:

The polyherbal formulation's antioxidant and hepatoprotective properties were shown to be dose-dependent, with larger dosages producing stronger results. Finally, the polyherbal formulation including extracts of Euterpe oleracea and Zephyranthes citrina demonstrated substantial antioxidant and hepatoprotective properties in Wistar rats. These results support the formulation's therapeutic potential in avoiding liver damage and oxidative stress-related diseases. However, further research is needed to understand the underlying mechanisms of action and to assess its effectiveness in clinical situations. PHFs include metabolites such as phenols, which inhibit pro-inflammatory pathways and cytokines. By lowering liver inflammation, these mixes may protect hepatocytes (liver cells) from possible damage (1, 24). Some flavonoids, including flavonols (quercetin and rutin), flavanones (hesperidin), flavanols (catechin), and anthocyanins (e.g., cyanidin), have been shown to have anti-inflammatory properties (25).

Detoxification assistance Certain herbs in polyherbal mixes may aid the liver's natural detoxification processes by improving detoxifying enzyme function and making it simpler for the body to eliminate toxins (1, 26). Stimulation of liver regeneration A fraction of the polyherbal mixes may enhance hepatocyte proliferation and division, possibly aiding in liver tissue regeneration. This system might help to repair damage produced by a variety of causes, including toxins and viruses (1, 27).

Polyherbal chemicals, such as flavonoids and terpenoids, have the ability to interact with a variety of cellular signaling pathways, including those involved in apoptosis (programmed cell death), cell survival, and proliferation. Polyherbs may help liver cells function better by regulating these pathways (1, 28). Chen et al. (29) shown that catalpol, a terpenoid, may significantly slow the evolution of liver disease and prevent fatty liver by suppressing inflammation and boosting lipid metabolism. Anti-fibrotic effects Liver fibrosis is characterized by excessive collagen buildup, which may lead to cirrhosis and reduced liver function. OS upregulates damaging cytokines such

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TGF-β, IL-6, and TNF-α, which contribute to fibrogenesis and the body's healing system (30). TGF-β stimulates ROS generation in endothelial and epithelial cells, followed by fibroblasts and other liver cells (9). Ingredients in PHFs may have the capacity to prevent fibrosis by inhibiting collagen production and accelerating its breakdown.

Immunomodulation

A variety of PHFs may influence the immunological response inside the liver, assisting in the modulation of immune cells and reducing liver damage induced by immune activity (31). Cholesterol control The contents of PHFs may help to regulate blood cholesterol levels and prevent fat build-up in the liver, lowering the risk of developing nonalcoholic fatty liver disease (32).

Polyherbal

Formulations have the ability to modulate the gut microbiota and the crucial gut-liver axis, both of which are critical to liver health. Polyherbals may indirectly benefit the liver by fostering a healthy gut microbiota (33). It is critical to understand that the particular processes of liver protection may vary depending on the distinct herbs and substances included in the polyherbal mix. Furthermore, further study is needed to fully understand the processes behind polyherbal medications' hepatoprotective properties and to determine their effectiveness and safety in a variety of conditions. Conclusion In this study, we covered a variety of PHFs designed to protect the livers and whose antioxidant activity has been evaluated.

The authors observed multiple PHFs owing to a lack of scientific validations and an increasing number of formulations. Such information disclosing their mechanistic technique or synergistic system is not easily accessible. The recorded research simply said that phenolics and flavonoids, which not only protect cells but also have antioxidant activity, might be responsible for PHFs' protective effect against hepatic damage.

As a result, it is possible that PHFs' capacity to serve as antioxidants in neutralizing toxic metabolites contributes to their hepatoprotective qualities. Interestingly, little or little information on these PHFs was identified. The quality and repeatability of formulations are not standardized. Although most herbal substances are regarded to be harmless, some plants may interact or have negative/allergic reactions when combined. Preclinical and clinical studies may reveal anti-inflammatory properties. PHFs include metabolites such as phenols, which inhibit pro-inflammatory pathways and cytokines. By lowering liver inflammation, these mixes may protect hepatocytes (liver cells) from possible damage (1, 24). Some flavonoids, including flavonols (quercetin and rutin), flavanones (hesperidin), flavanols (catechin), and anthocyanins (e.g., cyanidin), have been shown to have anti-inflammatory properties (25). Detoxification assistance Certain herbs in

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