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Review Article

Overview Of Hepatoprotective Activity of Polyherb

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ABSTRACT

The liver is a vital organ that plays a significant role in metabolism, detoxification, and maintaining homeostasis. Nearly 50% of acute liver failures worldwide are attributed to drug-induced liver injury (DILI). Acetaminophen, isoniazid, rifampicin, methotrexate, and some chemotherapeutic drugs are frequent hepatotoxic drugs. Drug-induced liver injury (DILI) ranks among the top causes of acute liver failure and continues to pose difficulties in contemporary pharmacotherapy. Due to their partial efficacy and potential toxicity, traditional hepatoprotective have generated curiosity regarding novel strategies. Due to their synergistic phytoconstituents' action on multiple mechanisms of liver protection and regeneration, herbal drugs, particularly polyherbal preparations, have been found to exhibit beneficial hepatoprotection. Pathophysiology and mechanism of drug-induced hepatotoxicity are discussed here, along with an overview of hepatoprotective activity of polyherbs. Herbs with antioxidant, anti-inflammatory, and membrane-stabilizing activity, e.g., *Ocimum sanctum*, *Emblica officinalis*, pure honey, and *Azadirachta indica*, receive special focus. To assure safety and efficacy, future perspectives highlight standardization, phytochemical profiling, and translational research.

INTRODUCTION

The liver plays a critical role in maintaining the normal metabolic homeostasis of the body and the biotransformation, detoxification, and excretion of various endogenous and exogenous compounds, including chemicals present in drugs and the environment.[1]

The whole body of knowledge, skills, and practices acquired from indigenous theories, beliefs, and experience is referred to as traditional medicine. It is utilized to prevent, diagnose, treat, and relieve physical and mental disorders as well as to preserve health. The most frequently employed form of traditional medicine is herbal therapy. Herbs, herbal material, herbal products, and processed herbal products with plant material or other plant parts as active components are all

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herbal medicines.[2] Liver disease has been prevented and treated for centuries with plants and natural materials worldwide. As shown by the vast number of research studies on the hepatoprotective potential of such herbal materials, scientific investigations have confirmed the therapeutic efficacy of their use. There are around 700 various plant-based mono and polyherbal preparations available for use.[3] The role of polyherbal formulations (PHFs) in hepatoprotection is increasingly gaining significance.

Herbs and plants are blended into polyherbal medicine to treat a variety of illnesses or to promote overall health. Numerous civilizations across the globe have been applying this Type of conventional medicine for centuries, and even today it is widely used. Together, numerous herbs in a blend enhance a synergistic effect, whereby the different constituents work together to enhance

therapeutic benefits while minimizing potential negative effects.[4]

PATHOPHYSIOLOGY OF DRUG-INDUCING HEPATOTOXICITY:

The two processes that make up the pathophysiology of DILI are intrinsic and idiosyncratic. [5][6][7] Drugs that are known to cause liver damage in a dose-dependent way with a brief latency period have an Intrinsic mechanism that is both predictable and reproducible. Acetaminophen toxicity, for example, leads to the formation of reactive metabolites which accumulate in excess to form hepatocyte necrosis and death.[5][8][9] Immune-mediated (allergic) liver injury due to hypersensitivity and non-immune-mediated metabolic (non-allergic) injury due to mitochondrial injury are the two types of idiosyncratic DILI mechanisms.[5][6].

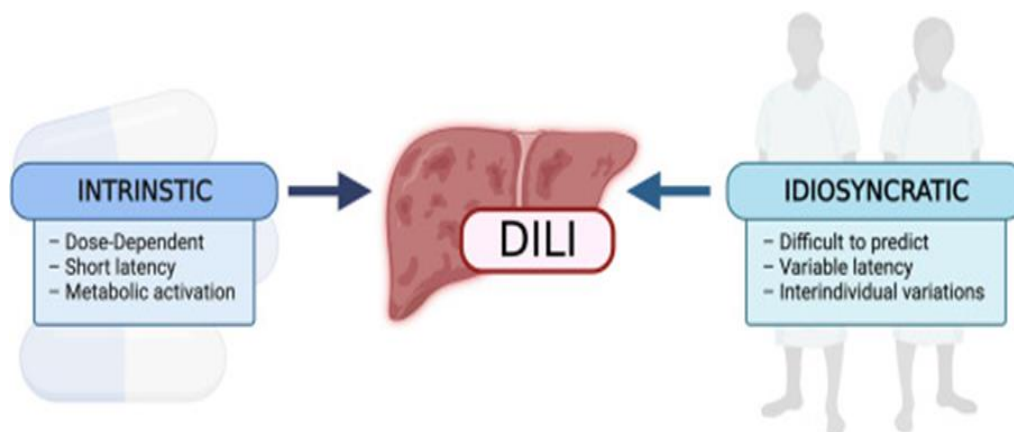


Figure: Pathophysiology of the drug-induced Hepatotoxicity

MECHANISM OF HEPATOTOXICITY:

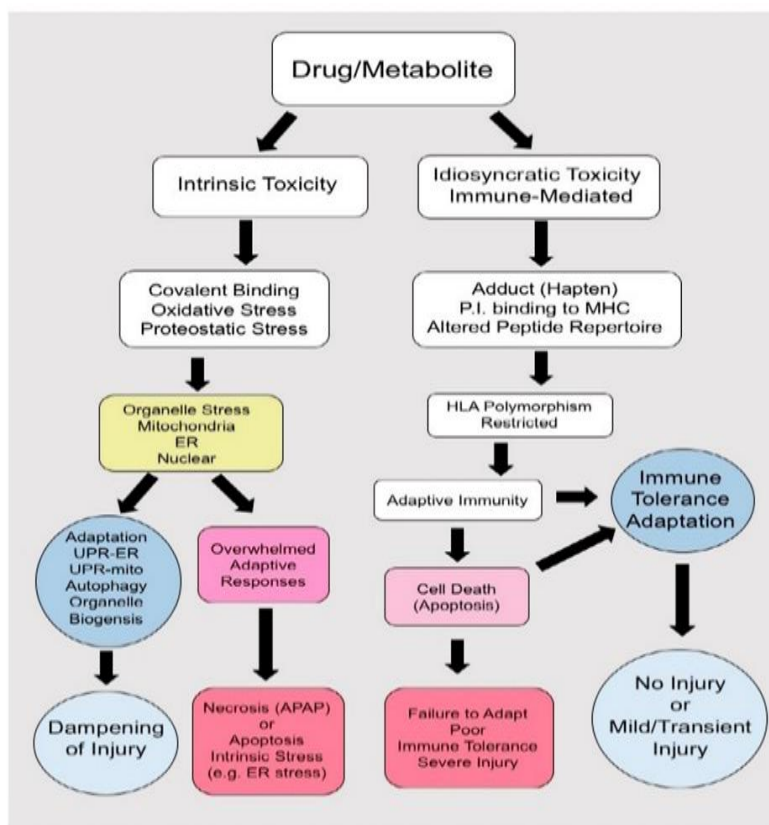


Figure: Mechanism of hepatotoxicity

Chemicals and their electrophilic metabolites commonly induce biochemical stress through covalent binding to or direct damage of mitochondria. The consequences can be oxidative stress, activation of stress signaling cascades, mitochondrial dysfunction, and endoplasmic reticulum stress. By modulating mitochondrial permeability transition (MPT) or mitochondrial outer-membrane permeability (MOMP), the ultimate cell death mechanisms all meet at the mitochondria. It is presently believed that drug-and/or metabolite-induced biochemical stress in the liver in genetically susceptible persons reveals the adaptive immune response's key role in disease, as attested by the robust HLA associations with idiosyncratic DILI. In making hepatocytes more vulnerable to the lethal effects of the immune response, the metabolic stress due to drugs can potentially enhance the degree of injury.[10]

Large doses of paracetamol, a pain-relieving and antipyretic drug used widely, have been reported to cause liver toxicity in animals and humans. Increased lipid peroxidation of the liver has been reported to be a general feature following exposure to hepatotoxins. [11] One of the mechanisms underlying carbon tetrachloride (CCl₄)-induced liver injury is oxidative stress, which also causes membrane disruption, loss of membrane-bound enzymes, and cell death. This is manifested as alterations in liver and plasma biochemical markers.[12] Long-term alcohol use leads to the accumulation of surplus fat within liver cells, causing more severe acute changes that can ultimately result in cell death. Acute inflammation, which contributes to liver conditions such as cirrhosis, is a major cause of mortality. [11]

HEPATOPROTECTIVE POLYHERBS:

Eugenol, flavonoids, and ursolic acid present in *Ocimum sanctum* leaves have been shown to have free radical scavenging activity and anti-liperoxidative activity.

Therefore, the hepatoprotective action of *Ocimum sanctum* leaves must be due to the antioxidant properties of their constituents.[13] The membrane-stabilizing ability of *Ocimum sanctum* is an important factor in its hepatoprotective action.[14] Fixed oil obtained from *Ocimum sanctum* contains linoleic acid, which is responsible for its anti-inflammatory activity. Thus, linoleic acid can also contribute towards reducing the inflammatory symptoms associated with liver damage, thus increasing its protective action on the liver.[15]

A 50 % fruit hydroalcoholic extract of *Embolia officinalis* possesses hepatoprotective activity against liver damage induced by anti-tuberculosis drugs. [16] It has also been demonstrated that *E. officinalis* possesses a hepatocurative effect on CYP 450 bioactivation hepatotoxicity. [17]

Honey is a thick, sweet, and sticky liquid created from nectar. It is mainly made up of water and carbohydrates. Also, it has trace amounts of different vitamins and minerals. They are calcium, copper, riboflavin, iron, magnesium, potassium, and zinc.[18] Honey is a good source of antioxidants because it is rich in polyphenols such as flavonoids and phenolic acids. Past studies have indicated that honey can provide multiple health benefits through the fight against various chronic diseases resulting from oxidative damage. It has the potential to provide protective effects against liver damage induced by chemical substances-induced oxidative stress.[19]

Medicinal plants and their constituents play an important role as hepatoprotective agents without having any side effects. An investigation was

carried out to study the hepatoprotective activity of azadirachtin-A against carbon tetrachloride (CCl₄)-induced hepatotoxicity in rats, and histological and ultrastructural observations proved that pre-treatment with azadirachtin-A appreciably reduced hepatocellular necrosis in a dose-dependent fashion.[20] The neem active fraction, nimbolide, exhibits a protective action against carbon tetrachloride (CCl₄)-induced liver toxicity in rats, proving that nimbolide affords effective hepatoprotection against CCl₄-induced liver damage.[21] The leaf extract has also been found to afford protection against paracetamol-induced liver necrosis in rats.[22] Conventional treatments for liver disease may be expensive and have potential side effects, so there is an increasing interest in using herbal remedies.

Herbal medicines, specifically designed herbal extracts, have been used for hundreds of years to treat a wide range of conditions, including liver diseases. The use of polyherbal formulations is becoming more common due to their potential combined effects, enhanced effectiveness, and improved safety when compared to single herb treatments. Although the popularity of polyherbal formulations is rising, there is a necessity for a thorough review of their liver-protective potential against various types of liver dysfunction.[23]

CONCLUSION:

According to the reviewed studies, polyherbal formulations have a significant hepatoprotective effect against a variety of hepatotoxic agents through a variety of mechanisms of action, including hepatocyte regeneration, immunomodulatory activity, anti-inflammatory, and antioxidant properties. Alkaloids, flavonoids, and polyphenols are examples of bioactive substances found in these formulations that have a variety of biological activities and aid in lowering oxidative stress, inflammation, and



immunological dysregulation, which contribute to liver damage. These results imply that polyherbal formulations could be a viable substitute for traditional medications in the management and prevention of liver disorders. To completely comprehend the mechanisms of action of these polyherbal formulations and identify the bioactive compounds, more research is necessary.

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