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Fruits And Vegetables Role In Prevention Of Hepatotoxicity

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ABSTRACT: Toxicology of the liver is a significant global health problem. The Food and Drug Administration withdraws several medications from the market due to drug-induced hepatotoxicity (FDA). This study purpose is to find out in-vitro activity of methanol extracts of different parts namely pulp, peel & seed of imported vegetables and fruits against CCl_4-induced hepatotoxicity. Suspension of Chicken liver cell was treated with CCl_4 and utilised to assess super oxide dismutase (SOD), free radical scavanging, and lipid peroxidation (LPO). The impact was strong, owing to the antioxidants included in extracts of several exotic fruits and vegetables. Indeed, methanolic extracts of specific unused components (peel and seed) of fruits and vegetables revealed hepatoprotective activity in this investigation, but the significant hepatoprotective activity was seen between all bottle gourd pulp (vegetable) and inactive fruit pulp (imported fruit). As a result, it was established that CCl_4-induced hepatotoxicity was detected with methanolic extracts of exotic fruits and vegetables.

KEYWORDS: hepatotoxicity; liver injury; paracetamol; carbon tetrachloride (CCl_4); thioacetamide (TAA); hepatoprotective agents.

INTRODUCTION: India is a culturally diverse and traditional country. This region has its own set of dietary customs and medicinal practises. In India, a variety of traditional medical methods, including folk medicine, tribal medicine, Ayurveda, Siddha, and Unani, rely on herbal resources for therapeutic purposes. However, it has been discovered that most of the plants and their components, such as leaves, seeds, fruits and medicinal rooted substances include antioxidants, flavonoids, tannins, and other phenolic compounds. The liver is essential for the performance, maintenance and control of homeostasis in the body. It comprises a range of metabolic growth pathways, illness management, nutrition storage and delivery. Additionally, it functions as a metabolic centre for the metabolism of nutrients such as proteins, lipids and carbohydrates, as well as the excretion of metabolic waste. Bile secretions, which is released by the liver, plays a crucial function in digestion. Maintaining a healthy liver is consequently critical for an individual's general well-being. Because the liver is so regenerative, there has been a steady rise in liver damage. Liver damage by drug-induced is most common creator of hepatotoxicity. Acute liver failure in children is caused by it in roughly 20% of cases, whereas the ALF rate in adults is greater, with an annual incidence of between 10 and 15 per 10,000 to 100,000 people who have been exposed to prescription medicines and drugs that cause ALF. Hepatotoxicity is one of the biggest issues in pharmacovigilance today, and it's the main reason people stop taking a drug because they think it's not safe. Researchers frequently employ in vivo and

vitro models to conduct their investigations. Chemical toxins can induce liver damage (including acetaminophen, carbon tetrachloride, galactosamine, and thioacetamide). A lot of hepatotoxic chemicals make lipid peroxidation more likely in the liver cells. The liver cirrhosis model that has been studied the liver cirrhosis caused by CCl_4. CCl_4 was the first toxin in which a free-radical mechanism was demonstrated to have a significant role in the damage produced. The cytochrome P450 enzyme breaks down CCl_4 into the radical, carbon-centered trichloromethyl. In a chain of events, first step is that leads to membranous lipid peroxidation (LPO) and cell death is thought to be the covalent binding of trichloromethyl free radicals to cellular proteins. ROS can damage cells and cause diseases like liver cirrhosis and fibrosis in humans. Reactive aldehydes, malondialdehyde (MDA), and 4-hydroxynonenal are some of the products that fatty acids break down into. These products are very easy to attach to protein working groups and stop a lot of enzyme activity. As a result of all of these changes, body cells die and TBARS and lactate dehydrogenase (LDH) leak out of them. The second phase of hepatotoxicity caused by CCl_4 is when Kupffer cells get activated and make mediators. If you want to study liver changes in terms of molecular, cell, and morphology, you can use CCl_4-hepatotoxicity as a good model. Hepatoprotection can be seen in extracts with a lot of free radical breakers and antioxidants. Additionally, they convert free radicals to waste products that are excreated and they have the capacity to repair cells that have been injured. Consumption of fruits and vegetables, on the other hand, has been demonstrated to reduce the chance of developing a variety of ailments. The health advantages are mostly attributed to phytochemicals like as polyphenols, carotenoids, and vitamins E and C. A variety of food-significant plants are employed as preventive substances for various diseases in Indian traditional medicine. Many vegetables are eaten without being aware of their medicinal properties. Some vegetables and fruits that have been reported to have significant hepatoprotective activity. These were analysed by hepatotoxicity inducer and biochemical parameters studied.

Hepatoprotective Activity of Some commonly consumed vegetables (in the form of seeds, roots, leaves and fruits)

In Indian traditional medical practice a variety of food significant plants are used as preventive substances for diverse ailments. Many vegetables are consumed without the realization of the medicinal values. However, a list of plants reported to have significant hepatoprotective activity, in alphabetical order of their family, together with their scientific names, plant part consumed, type of extract used in assay, Hepatotoxicity inducer, biochemical parameters studied and references.

Biochemical Parameter studies:

The majority of hepatotoxic substances cause liver cell damage primarily through lipid peroxidation and other oxidative stress. Estimation of the alkaline phosphatase (ALP), total protein (TP), alanine aminotransferase (ALT), albumin (ALB), aspartate aminotransferase (AST), glutathione (GSH), total bilirubin (TB), Gamma-glutamate transpeptidase (GGTP), malondialdehyde (MDA), Total Glyceride (TG), Serum glutamate oxaloacetate transaminase (SGOT), Serum glutamate pyruvate transaminase (SGPT) and Reactive Oxygen species (ROS) (superoxide dismutase, catalase) with the levels of control animals and micrographs on histopathological changes were used in general as diagnostic tools.

Allium cepa L

Rawat et al. [4] investigated onion bulbs and their extract for their hepatic protective activities in wistar albino rats after causing liver damage with CCl_4, ethylacetate, and paracetamol. After bio-activation to a hazardous electrophile, cytochrome P450 monooxygenase generates N-acetyl-p-benzoquinone-imine (NAPQI) in high levels of liver necrosis (a microsomal enzyme). The SGOT and SGPT levels shift as a result of this. As a result of CCl_3's enzymatic activation, many levels of ALP, SGPT, bilirubin and SGOT have elevated dramatically. The raised biochemical parameters of the alcoholic extract (AEAC) and aquatic extract (AQEAC) treatments were dramatically lowered in this study because saponins, carbohydrates, steroids, and flavonoids interfere with the cytochromome P450 monooxygenase, lowering hepatotoxic-free radicals. Liver histology has also demonstrated the extracts' hepatoprotective properties. Ige et al. used male Wistar rats as a model to demonstrate the preventative efficacy of allium cepa aqueous extract (ACE) against cadmium-induced hepatotoxicity. The hepatotoxic impact of Cd is shown to cause accumulated oxidative damage. Cadmium is found in the livers of all groups of rats exposed to Cd, which causes superoxide dismutase (SOD) to decrease and malondian dehydration to rise (MDA). serum aspartate aminotransferase levels [8]. ALT, AST, and ALP are the most frequent enzymes used to detect hepatocellular injury. The activity of these enzymes in the plasma increases as a result of hepatic injury. AcE's capacity to retain the integrity of hepatocytes and ROS scabbing reduces hepatotoxicity caused by Cd.

Allium sativum L

The hepatoprotective effect of garlic supplemented diets with Vitamin-C against lead-induced hepatotoxicity in experimental study was done on rats by Ajayi et al. and Senapati et al. [9-10]. Due to lead therapy, they noticed a significant rise in ALT and ALP enzyme levels, as well as a decrease in AST, indicating liver damage. After-leading Allium sativum and vitamin C treatments lowered ALT and ALP activities while increasing plasma AST activity, which was comparable to control activities. The cysteine-containing enzymes are known to bind to sulfhydrate groups, and complexes with amino acids and protein have been discovered. Because ALT is a liver enzyme, the plasma discharge into the blood [11-12] disrupts the tissue's membrane, changing the tissue level. The inverse impact of plum hepatotoxicity is attributed to lower serum activity of ALT and ALP, which is linked to decreased synthesis of these enzymes. Ebenyi et al. (14] on Paracetamol and other studies were carried out in a similar manner [13] on Paracetamol by Md. Asaduzzaman and al. [15] on Islandazid.

Amorphophallus paeoniifolius

Methanol and aqueous extracts of the elephant foot yam tuber and its hepatoprotective activity in male albino-wistar rats, causing liver damage from Paracetamol, were investigated by Pramod J Hurkadale et al. [16]. The metabolite N-acetyl-p-benzoquinoneimine (NAPQI) reaction is triggered by paracetamol hepatotoxicity, which results in oxidative stress and lutathione depletion. It's a well-known pyretic and analgesic that induces liver necrosis at larger dosages. Rats were pre-treated with aqueous extract and methanol prior to receiving paracetamol resulted in substantial reductions in silymarin and Liv-52 nearly comparable ALP, SGOT, SGPT and SB values ($P<0.01$). A histopathologic test of the controlling liver tissue and amorphophallus extract treated animals was confirmed for hepatoprotective action. Histopathology reports reveals that steroids and flavonoids were accountable for hepatoprotection, as the major chemical constituents of the tubers are carbohydrates, sitosterol, stigmasterol, thiamines and riboflavins.

Benincasa hispida (BH)

Bort et al. [22] discovered diclofenac hepatotoxicity in hepatocytes. The hepatoprotective effects of aqueous winter melon (BH) extract in male albino rats against diclofenac-sodium-induced liver injury were reported by Das, S.K. and C. Roy [23]. Activities reduced levels in superoxide dismutase (SOD), serum glutamate pyruvate transaminase (SGPT), catalase (CAT), serum glutamate oxaloacetate (SGOT), glutathione (GSH), alkaline phosphatase (ALP) & lipid peroxidation (LPO) induced by diclofenac sodium were found to have a hepatoprotective effect. The BH pulp contains vitamin E, beta-carotene, flavonoids, and flavonols. The findings of SGOT, GSH, LPO, CAT, ALP, SOD, and SGPT activities, as well as the presence of vitamin E, beta carotene, flavonols, and flavonoids in BH pulpe, are inferred as BH protected rat's liver from oxidative stress. BH hepatoprotection from nimesulide-induced hepatotoxicity was also found by Das and Roy.

Carica papaya:

Rajkapoor et al. [32], Md. Zafor Sadeque et al. [33], and Manikandaselvi et al. [34] evaluated the anti-hepatotoxic effect of ethanol and aqueous extracts in Carica papaya on CCl_4-induced hepatotoxicity. Aspartate aminotransferase, Total bilirubin, Alanine aminotransferase, (AST), Alkaline phosphatase & gamma-glutamate transpeptidase were some of the biochemical tests used to evaluate activity. Hepatoprotective activity was tested for Carica papaya seed extract, which was compared to a control liver sample for histological changes [35]. Srinivasan Kantham investigated the impact of carica papaya aqueous extract on paracetamol (PCM) and thioacetamide (TAA) caused liver damage in rats. Wistar strain albino rats were given three dosages of CPE (100, 250, & 500 mg/kg p.o.) as a prophylactic treatment for 10 days, and liver damage was then produced. Biomarkers were used to assess hepatoprotective capacity, and hepatoprotection activity was determined. It's believed Vitamin C is considered to be responsible for the protection.

Citrus limon:

Bhavsar et al. Studied HepG2 cell line [37] by examining ethyl acetate soluble fraction of the extract and ethanol extract of Lemon fruit for its effects on CCl_4-induced hepatotoxicity. The ethanol extract was shown to normalise the increased levels of liver enzymes, total and direct bilirubin in rats exposed to carbon tetrachloride. Treatment dramatically decreased malondialdehyde (MDA) levels in liver tissue, hence reducing lipid peroxidation, and increased antioxidant enzyme levels [38]. Also, reduced glutathione (GSH) levels were increased in treated rats compared to CCl_4-induced rats. Thus, it may be deduced that antioxidant enzymes offered hepatoprotection through their ROS activity. Casimiro et al. 2010; Karaca [39], utilising Citrus bergamia.

Vigna mungo

Nitin et al. [123] demonstrated that a alocoholic extract of seeds of Vigna mungo (AEVM) protected adult albino rats' livers from ethanol-induced hepatic injury. After exposure to ethanol, it was observed that liver mass and volume, serum enzymes increased, (oxaloacetate transaminase, total bilirubin, glutathione pyruvate transaminase and alkaline phosphatase) and thiopentone levels enhanced. AEVM treatment substantially lowered the levels of the enzymes SGPT, SGOT, ALP, and BIT on comparion to the ethanol control group. Extract may have hepatoprotective effect due to the presence of powerful diuretics such as saponins and strong antioxidants such as ascorbic acid, total phenolic compounds, tannins, and flavonoids [124-125]. Anitha et al. [126] examined and confirmed Vigna mungo's hepatoprotective effects against CCl4-induced hepatotoxicity. Solanki et al. [127]

investigated and confirmed that Vigna mungo provides equivalent hepatoprotection against acetaminophen and CCl_4-induced hepatotoxicity.

FRUIT AND VEGETABLE EXTRACT PREPARATION:

Fresh imported fruits (Table 2.1a) and vegetables (Table 2.1b) were obtained from hopcoms and cleaned under running tap water before separating the skins, pulp, and seeds. They were separately shade dried for almost a month. A mechanical grinder was used to grind the dried fruit pieces. Each sample was roughly weighed before being extracted by cold maceration with 80 percent methanol at RT for 72 hours and the macerate was immersed in 80 percent methanol. After 72 hours, the samples were filtered using filter paper and obtained methanol extracts were collected in vials and kept at 4°C.

Table 2.1a: List of Exotic Fruits Used

Exotic Fruits	Scientific Name
Date Palm	Phoenix Dactylifera
Grape Vine	Vitis Vinifera
Passion Fruit	Passiflora Edulis
California Wild Grape	Vitis Californica
Kiwi Fruit	Acinidia Deliciosa
Wood Apple	Limonia Acidissima
Indian Jujube	Ziziphus Mauritiana
Avocado	Persea Americana
Litchi	Litchi Chinensis
Java Plum/Black Palm	Syzygium Cumini
Rose Apple	Syzygium Jambos
Soursop	Annona Muricata

Table 2.1b: List of common Vegetables Used

Common Vegetables	Scientific Name
Egg plant	Solanum melongena
Bitter gourd	Momordica charantia
Ivy gourd	Coccinia grandis
Tomato	Solanum lycopersicum
Green chilli	Caosucyn frutescens
Ladies finger	Abelmoschus esculentus
Cucumber	Cucumis sativus
Bottle gourd	Lagenaria siceraria
Bell peppers	Capsicum annuum
Snake gourd	Trichosanthes cucumerina

Significant results were found in all of the plant samples including various fruit and vegetable extracts. When compared to other fruit extracts, extracts from the peel of litchi and California grapes were suppress lipid per oxidation quite efficiently. The efficiency was reduced with Black plum and passionate fruit. In comparison to peel extracts from other parts, peroxidation has been found to be extremely inhibited by the vegetable peeling of brinjal and cucumber, but ladies finger have little effect. In addition to the peel extract, the pulp extracts showed LPO inhibitions. A stable free radical, DPPH was used to determine the radical scavenging abundance of fruit and vegetables. The present study showed high levels of free radical scavenging among all other vegetables: snake

gourd seeds, bottle gourd pulp, and brinjal peel; the activity of free radical against ascorbic acid was a positive standard in the fruit, litchi peel, passion fruit pulp, and rose apple seeds.

CONCLUSION:

This paper describes the hepatoprotection of entire plant extracts (peel, pulp, seed) from common vegetables and exotic fruit. All the extracts with powerful hepatotoxicity actions have been shown. This was concluded by the above results, which showed a significant anti-hepatotoxic effect for CCl_4 induced liver toxicity in in-vitro conditions of exotic fruit and common vegetable extracts.

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