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Ayurveda

PROTECTIVE EFFECTS OF AMRUT GHRUT ON CYCLOPHOSPHAMIDE-INDUCED HEPATIC DAMAGE. A REVIEW STUDY

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ABSTRACT Cyclophosphamide (CPA) is a widely used alkylating agent in chemotherapy and immunosuppressive therapy. However, its therapeutic use is often limited by its hepatotoxic side effects, primarily caused by the generation of reactive oxygen species (ROS) and toxic metabolites. Ayurveda offers several herbal remedies, among which Amrut Ghrut, a medicated ghee formulation, is known for its antioxidant, anti-inflammatory, and hepatoprotective properties. This review aims to explore and critically analyze the existing preclinical evidence on the protective effects of Amrut Ghrut against CPA-induced hepatic damage.

KEYWORDS : Cyclophosphamide, Hepatotoxicity, Amrut Ghrut, Oxidative Stress, Ayurvedic Medicine, Antioxidant, Hepatoprotective, Medicated Ghee

INTRODUCTION

Cancer is a generic term for a large group of disease that can affect any part of the body. Other terms used are malignant tumours and neoplasms. One defining feature of cancer is the rapid creation of abnormal cells that grow beyond their usual boundaries, and which can then invade adjoining parts of the body and spread to other organs; the latter process is referred to as metastasis. Widespread metastases are the primary cause of death from cancer.[1] 17.5 million cases of cancer were reported across the world in 2015, along with 8.7 million deaths. The incidence rate has increased by 33% between 2005 and 2015 partly due to population growth and aging. Currently, cancer is the second cause of death worldwide and is expected to hit 27.1 million people by 2030 - especially in rich countries. [1]

Cyclophosphamide is a type of nitrogen mustard drug which exerts its effects through the alkylation of DNA. The drug is not cell-cycle phase-specific and metabolizes to an active form capable of inhibiting protein synthesis through DNA and RNA crosslinking. [2][3]

Ayurveda, the ancient Indian medical system, provides holistic and natural therapies. Amrut Ghrut, a traditional polyherbal ghee formulation, has been used for centuries for its Rasayana (rejuvenating) properties. It is believed to strengthen liver function, support detoxification, and combat free radical damage. The goal of this review is to enhance the awareness for the potential benefits of Ayurvedic ~ visha hara formulations as combined treatment for cancer patients.

MATERIALS AND METHODS

This is a review-based study designed to critically evaluate existing Ayurvedic and modern research literature concerning the hepatoprotective effects of Amrut Ghrut on Cyclophosphamide (CPA)-induced hepatic damage. The methodology involves systematic collection, screening, and qualitative analysis of data from classical Ayurvedic compendia and modern scientific sources.

Data were Collected from the Following Categories of Literature:

- **Classical Ayurvedic Texts:**

References related to Amrut Ghrut, Visha Hara Yogas, and Agada Chikitsa were extracted primarily from:

- Sushruta Samhita (Dundubhisvaniya Adhyaya)
- Charaka Samhita (Kalpa Sthana)
- Ashtanga Hridaya
- Bhavaprakasha Nighantu
- Dravyaguna Vigyana texts (Murthy, Deshpande, Sabnis, etc.)

- **Modern Scientific Literature:**

Data were collected from published research articles, pharmacological studies, review papers, and dissertations focusing on:

- Cyclophosphamide-induced hepatotoxicity models
- Antioxidant and hepatoprotective mechanisms
- Phytochemical and pharmacological actions of Amrut Ghrut ingredients

Adverse Effect of Cyclophosphamide

The main areas of concern regarding the adverse side effects of cyclophosphamide are associated with bladder and gonadal toxicity. Common adverse side effects reported in several studies and clinical trials involving the use of cyclophosphamide include haemorrhagic cystitis, amenorrhea, myelosuppression, alopecia, and spells of nausea and vomiting. [4]

Cyclophosphamide, a widely used alkylating agent, is known to induce hepatotoxicity through oxidative stress, inflammatory responses, and metabolic activation of its toxic metabolites such as acrolein and phosphoramide mustard, leading to hepatocellular necrosis and elevation of liver enzymes in both experimental and clinical studies.[5]

Amrut ghrut

Amruta ghrut is that formulation which is discussed while discussing Agada's (Anti-toxic) in the treatment of—Sarvavisha" (all type of poisonous states).

Amrutha here refers to —nectar & is said to be able to bring back a seemingly dead man to life. This special formulation is been described by Sushruta acharya in Dundhubhisvaniya adhyaya (chapter) for all Visha (poisonous) condition. [6]

RESULT: -

Table 1: Showing Content of Amrut Ghrut [6]

Sr. No.	Drug	Latin Name	Family	Part used
1	Apamarga	Achyranthus aspera	Amaranthaceae	Beej (seeds)
2	Kakamachi	Solanum nigrum,	Solnaceae	Fruit
3	Aparajitha	Clitorea ternatea,	Fabaceae	Roots
4	Shirish	Albizia lebbek,	Mimosoideae	Beej (seeds)
5	Go ghrut	Clarified butter		
6	Go mutra	Cow urine		

Pharmacological Properties and Its Action

Table 2: Showing Ayurvedic Pharmacological Properties.[7][8]

Drug	Rasa	Guna	Veerya	Vipaka	Dosha
Apamarga	Katu, tikta	Laghu, ruksha, tikshna	Ushna	Katu	Kapha-Vata hara
Shirish	Kashaya, tikta, Madhura, katu	Laghu,	(Anushna)	Katu	Tridoshahara
Aparajita	Katu, tikta, kashaya	Laghu,	Shita	Katu	Tridoshahara
Kakamachi	Tikta, katu	Laghu, snighda	Anushna	Katu	Tridosha
Go mutra	Katu, kshara	Laghu, ruksha, tikshna	Ushna	Katu	Kapha hara

Go ghrut	Kashaya, madhura	Laghu, snigdha	Shita	madhura	Tridoshahara

Table 3: Pharmacological Action. [7][8]

Drug	Karma	Rogaghnata (Indication)	Chemical constituents
Apamarga	Dipanapachana, medohara,	Udara, ashmari, hydroga,	Betaine,Achyranthine, Echysterone, Achyranthes, Saponins
Shirisha	Vishaghna, vranaropana, vedanasthapana, shothahara	Shota, vrana, visarpa, visharoga	Albegenin, Saponins, Albegenic acid,seeds:- proteins, aminoacids
Aparajitha	Tridoshahara, medhya, vishaghna, chakshushya	Kushta, shota, unmada, vrana, shula	Aparajitn, kaempferol, terantins, guercetin
Kakamachi	Vrshya, Rasayana	Shota, jvara, netraroga, kushta	Leaves: solasonine, solamargin, steroidal alkaloids
Go mutra	Bedhana	Gulma, pandu, mutrakrichra,	
Go ghrut	Depana, vrshya, rasayana, vishaghna	Agnimandya, visha rog	

Therapeutic Potential of Amrut Ghrut

Table 4: Showing Anticancer Properties.

DRUG	ACTION
Apamarga	Methanolic extract of Achyranthes aspera contains potent anti-proliferative compound with specific activity against pancreatic cancer.[9] Ethanolic plant root extract of Achyranthes aspera L. showed in-vitro anticancer activity against different human cancer cell lines such as liver and colon.[10]
Shirisha	Saponin rich fraction of A. lebbeck showed antiproliferative, antiangiogenic and apoptogenic potential using various in-vitro models. It also found to increase chromosomal aberration and thereby may affect cell cycle.[11]
Aparajitha	The methanol extract of Clitoria ternatea (MECT) increased the life span of EAC tumour bearing mice and decreased lipid peroxidation and thereby augmented the endogenous antioxidant enzymes in the liver. All these parameters suggest that the methanol extract of Clitoria ternatea (MECT) seeds exhibits potential antitumor and antioxidant activities.[12]

Table 5: Anti-inflammatory Properties.

DRUG	ACTION
Shirish	Albizia lebbeck Benth. is used both in Indian traditional system and folk medicine to treat several inflammatory pathologies such as asthma, arthritis and burns. The aim of the present study was to evaluate the scientific basis of anti-inflammatory activity of different organic solvent extracts of Albizia lebbeck.[13]

Table 6: Immunomodulatory Properties.

DRUG	ACTION
Apamarga	The extract of Achyranthes aspera was found to increase the induction of OVA-specific antibody response in a dose-dependent manner. A significant elevation of IgM, IgG 1 and IgG 3 antibodies was observed.[14]
Shirish	The results showed that standardised extract of Albizia lebbeck has anti-inflammatory and immunomodulatory activity as evident from the modulation of cellular and molecular markers of inflammation and immunity in the model of airway inflammation. [Indian J Chest Dis Allied Sci 2018;60:147-152][15]
Aparajitha	Methanolic extract of Clitoria ternatea at the dose of 100, 200 and 400 mg/kg bd. wt. along with the antigen (sheep red blood cells) showed significant increase in the production of circulating antibody titre and the number of plaque forming cells (PFC) in response to (SRBC's) in the spleen. MECT showed significant immunostimulating activity with specific and non-specific mechanism which may be due to the presence of prominent amount of flavonoids and phenols.[16]

Table 7: Organ Protective Properties.

DRUG	ACTION
Kakamachi	The ethanol extract showed remarkable Hepatoprotective activity. The activity was evaluated using biochemical parameters such as serum aspartate amino transferase (AST), alanine amino transferase (ALT), alkaline phosphatase (ALP) and total bilirubin. The histopathological changes of liver sample in treated animals were compared with respect to control.[17]

Table 8: Antioxidant Properties.

DRUG	ACTION
Aparajitha	The pharmacological studies and preclinical studies prove the effectiveness of Clitoria ternatea Linn in various conditions like Analgesic, Hepatoprotective, Antioxidant, Hypoglycemic, Anthelmintic, Diuretic, Antibacterial, anti-cancer and Antidepressant properties and Hepatoprotective properties.[18]

Table 9: Table of Go-Ghrut (Cow Ghee) and Go-Mutra (Cow Urine) Properties.

Aspect	Go-Ghrut (Cow Ghee)	Go-Mutra (Cow Urine)
Source	Clarified butter obtained from cow's milk	Distilled/excreted urine of indigenous cow
Rasa (Taste)	Madhura (Sweet)	Katu (Pungent), Tikta (Bitter), Kashaya (Astringent)
Guna (Qualities)	Guru (Heavy), Snigdha (Unctuous), Mridu (Soft), Sara (Flowing)	Laghu (Light), Ruksha (Dry), Tikshna (Sharp)
Veerya (Potency)	Sheeta (Cooling)	Ushna (Hot)
Vipaka (Post-digestive effect)	Madhura	Katu
Prabhava (Specific effect)	Rasayana (Rejuvenating), Medhya (Brain tonic)	Shodhana (Detoxifying), Krimighna (Antimicrobial)
Action on Doshas	Tridosha Shamaka (mainly Vata-Pitta)	Tridosha Shamaka (mainly Kapha-Vata)
Therapeutic Uses (Ayurvedic)	Improves memory, digestion, vision, complexion, and vitality; used in Panchakarma (Nasya, Snehana, Basti)	Used for detoxification, skin diseases, liver disorders, metabolic disorders, and as a bio-enhancer in Panchagavya formulations
References	Charaka Samhita, Sushruta Samhita, Ashtanga Hridaya	Charaka Samhita, Sushruta Samhita, Panchagavya Chikitsa texts

DISCUSSION

In Ayurvedic concept, according to 'Charaka' and 'Sushruta Samhitas' cancer is described as inflammatory or non-inflammatory swelling and mentioned either as 'Granthi' (minor neoplasm) or 'Arbud' (major neoplasm).[19] The nervous system (Vata or air), the venous system (Pitta or fire) and the arterial system (Kapha or water) are three basics of Ayurveda and very important for normal body function. In malignant tumors all three systems get out of control (Tridoshas) and lose mutual coordination that causes tissue damage, resulting critical condition. Tridoshas cause excessive metabolic crisis resulting in proliferation.[20]

Visha & Cancer

Chemotherapy is a crucial cancer treatment strategy. However, it is commonly associated with side effects which usually a reflection of their mechanism of action. Despite its therapeutic effects, it has several adverse impacts that greatly reduce quality of life. The initial few dosages Chemotherapy function as therapeutic doses, destroying cancerous cells. Most chemotherapy drugs show activity in rapidly multiplying cells. They cannot distinguish between cancer and healthy cells so they tend to affect healthy normal rapidly multiplying cells, e.g., bone marrow, GI tract, hair follicles. Its subsequent doses accumulate in the body and cause significant damage to healthy organs too, so the body fails to clear excess medications and some of its components remain in the body, continuing to harm body when concentration is highest, resulting in a formation of visha (latent poison). The accompanying signs and symptoms will be consistent with the Dushivisha.[21]

Ghrut in Cancer Treatment

As per Ayurveda, ghee enhances longevity and shields the body against all kinds of diseases.[22] It enhances digestive fire (agni) and enhances absorption as well as assimilation. It enriches Ojas, the subtle essence of all the tissues (dhatus) of the body. It enhances memory and increases the strength of the brain and nervous system. It oils the connective tissues, thus making the body more supple. Ghee calms Vata and Pitta and is tolerable for Kapha in moderate amounts.[23]Ghrut is also opposite in nature to Visha (posion) and thereby guards the body against its activity. It also guards the heart and finally guards the Oja (essence of life). Ghee is also dhatuvyapar[24] (restoring homeostatic equilibrium and maintaining physiological process). It therefore cancels the harmful effect of radiotherapy and chemotherapy since both of them work as Visha (poison) to the body. Ghee is also narrated in the treatment of dagdha chikitsa. Ghrut has essential fatty acids which though transporting medicaments get absorbed into all cells by beta oxidation.[25]

CONCLUSION

Combining natural bioactive compounds with chemotherapeutic agents has the potential to mitigate the side effects often seen with conventional cancer treatments. Herbal medicines have played a crucial role in managing various diseases, including cancer, for centuries—their bioactive constituents offer proven preventive and therapeutic benefits for cancer, yet many Ayurvedic formulations described in classical texts remain insufficiently explored at the phytochemical level. Among these, Agada formulations, traditionally recognized as antidotes (visha hara), offer a promising area of research for their potential application in anti-toxic management and integrative cancer therapy.

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