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HEPATOPROTECTIVE POTENTIAL OF BILWADI AGADA – A REVIEW

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ABSTRACT

Bilwadi Agada is explained as one of the formulations in the context of Ayurvedic snake bite management. It is indicated in various conditions such as *Bhujanga Visha* (snake bite), *Luta Visha* (spider poison), *Unduru Visha* (rat bite), *Vrischika Visha* (scorpion sting), *Visuchika* (Cholera), *Ajirna* (indigestion), *Gara Visha* (artificial poison), *Jwara* (fever) & it has also got *Bhutaghna* properties (antimicrobial, antiviral).The liver is the common target organ for the effect of toxic compounds especially direct toxic effects because of – Its structure, role in intermediary and xenobiotic metabolism, position and function. Indiscriminate uses of drugs like tetracycline, acetaminophen, anti-tubercular drugs, oral contraceptives of hormonal origin, food preservative and agrochemicals are threatening the liver. Further addiction to alcohol and other drugs have aggravated the problem. The presence of hepato-protective drugs in Bilwadi as well as its indication in poisoning makes it a prime candidate for demonstrating hepatoprotective activity.

Keywords: *Bilwadi Agada*, Liver, Hepatoprotective

INTRODUCTION

Bilwadi Agada is explained as one of the formulations in the context of Ayurvedic snake bite management.[1]*BilwadiAgada* is indicated in various conditions such as *Bhujanga Visha* (snake bite), *Luta Visha* (spider poison), *Unduru Visha* (rat bite), *Vrischika Visha* (scorpion sting), *Visuchika* (Cholera), *Ajirna* (indigestion), *Gara Visha* (artificial poison), *Jwara* (fever) & it has also got *Bhutaghna* properties (antimicrobial, antiviral).[2]

As per the western science, any toxic compound after entering biological system has to undergo 4 phases namely Absorption, Assimilation, Metabolism and Excretion. Majority of the compounds ingested enters into the portal vein supplying the liver with blood from G.I. tract. Thus, liver becomes the common target organ for the effect of toxic compounds due to – Its structure, role in intermediary and xenobiotic metabolism, position and function. Hepatocytes, make up the majority of liver

structure are metabolically very active, and interference with such essential intermediary metabolic activity by exogenous chemicals may result in toxicity. Unsystematic uses of synthetic drugs like tetracycline, acetaminophen, anti-tubercular drugs, oral contraceptives of hormonal origin, food preservative and agrochemicals threaten the liver. Further addiction to alcohol and other drugs have aggravated the problem. [3]

MATERIALS & METHODS

The study being a literary review, the sources of data will have collected from all *Brihat* and *Laghu* Trayees also from all Contemporary Textbooks, Relevant Journals and Websites.

Conceptual Review

Yakrut in *Ayurveda*

Brihadaranyaka Upanishad mentions the anatomical site of the *Yakrut* below and right to the *Hrudya*, which is hard in texture. Arunadatta explains that *Yakrut* is considered as one of the *Koshtanga* and is a *matruja avayava* formed from *samanavata*, *dehoshma* and *rakta*. In *Veda Yakrut* is called as Takima or yakna.[4] Shabda stoma mahanidhi clarifies that because it causes Sanyama (check or control) it is called as *Yakrut*.

According to Acharya Sushruta, the *utpatti* of *yakrut* and *pleeha* is by *rakta*[5]. Its functions are mainly ascribed towards *rakta*. It has been mentioned as *moola* of *raktavaha sira/srotas* and seat for *raktadharakala*, *Ranjakagni* and *Pitta* also. The *rasa* when reaches *Yakrut* and *pleeha* being acted upon by *Ranjakagni* forms *sthularakta*, *malapitta* and *sukshma mamsa*.[6]

Yakrut and *pleeha* are considered as the *moola* of *rakta*vaha*srotas*. From the above description, we can infer that *yakrut* and *rakta* have a (*Samavaya*) relation. Therefore, vitiation of *Rakta* will also result in derangement in the functions of *Yakrut* and vice versa.[7]

Liver diseases - A modern approach[8]

Liver plays a crucial role in regulation of physiological processes. It is involved in several vital functions such as metabolism, secretion and storage. Detoxification of a variety of drugs and xenobioticalso occur in liver. Liver diseases mainly occurs due to exposure to toxic chemical substances like, antibiotics, chemotherapeutics, aflatoxin, acetaminophen, carbon tetra chloride, chlorinated hydro carbons, varied infections, auto immune disorders and also due to chronic alcoholism. Most of the hepato toxic chemicals damages liver cells mainly by inducing lipid peroxidation and other oxidative damages takes place in liver.

Toxic and Drug Induced Hepatitis[9]

Drug induced hepatitis is the inflammation of the liver with symptoms similar to viral hepatitis, but one difference it is caused by medication not a virus.

Liver injury may follow the inhalation, ingestion, or parenteral administration of a number of pharmacologic and chemical agents. These include industrial toxins (eg. Carbon tetrachloride, Trichloro ethylene, and yellow phosphorous), the heat-stable toxic bicyclic octapeptides of certain species of Amanita and Galerina hepatotoxic mushroom poisoning and more commonly, pharmacologic agents used in medical therapy (acetaminophen).

As the major drug metabolizing and detoxifying organ in the body, the liver is subject to potential damage from an enormous array of therapeutic and environmental chemi-

cals. Injury may result (1) from direct toxicity (2) via hepatic conversion of xenobiotic to an active toxin. (3) Through immune mechanism, usually by the drug or a cellular protein in to immunogen.

Table 1: Showing principle alterations of Hepatic morphology produced by some commonly used drugs and chemicals.[10]

Principal Morphologic Change	Class of Agent	Example
Cholestasis	Anabolic steroid, Anti-inflammatory Antibiotic Oncotherapeutic Oral contraceptive	Methyl testosterone Sulindac Erythromycin estolate, rifampcin Busulfan, tamoxifen Norethynodrel with mestranol.
Fatty liver	Antibiotic Antiviral Oncotherapeutic	Tetracycline Dideoxynucleosides Asparaginase, methotrexate
Hepatitis	Anticonvulsant Antihypertensive Anti-inflammatory Anti fungal	Phenytoin, carbamazine Methyldopa, captopril Indomethacin, Ibuprofen Fluconazole, Ketocanazole
Toxic (necrosis)	Metal Hydrocarbon Analgesic	Yellow phosphorous Carbon tetrachloride Acetaminophen
Granulomas	Anti-arrhythmic Anti-biotic	Quinidine Sulfonamides

Classification of Hepatotoxic Agents

Hepatotoxins can be classified into the following classes depending on the source of the toxin. They are,

1. Natural Origin – eg. Tannic acid, Aflatoxin, Pyrrelidizone alkaloids, Gyrometrin.
2. Synthetic Origin –
   (a) Toxins of clinical significance eg. Sulfonamides, PAS, Rifampicin etc.
   (b) Toxins having pathologic significance eg. Chloroform, Tetrachlorethane etc.
   (c) Toxins used as a common lab models eg. Carbon tetrachloride, Galactosamine.[11]

Table 2: Showing *Bilwadi Agada* and its Ingredients

Sl. No	Drug	Scientific name	Family	Parts used	Quantity
1	*Bilwa*	Aegle marmelos corr	Rutaceae	Root	1 part
2	*Surasa*	Ocimum sanctum Linn	Lamiaceae	Flower	1 part
3	*Karanja*	Pongamia pinnata Linn	Fabaceae	Seed	1 part
4	*Natam*	Valeriana wallichi DC	Valeriaceae	Root	1 part
5	*Devadaru*	Cedrus deodara Roxb	Pinacae	Heart wood	1 part
6	*Hareetaki*	Terminalia chebula Retz	Combrietaceae	Fruit	1 part

7	*Vibheetaki*	Terminalia bellerica Roxb	Combrietaceae	Fruit	1 part
8	*Amalaki*	Embica officinalis Guartn	Euphorbiaceae	Fruit	1 part
9	*Shunti*	Zingeber officinale	Zingeberaceae	Rhizome	1 part
10	*Maricha*	Piper longum Linn	Piperacae	Fruit	1 part
11	*Pippali*	Piper niagrum Linn	Piperacae	Fruit	1 part
12	*Haridra*	Curcuma longum Linn	Zingeberacae	Rhizome	1 part
13	*Daruharida*	Berberis aristata D	Berberidaceae	Stem	1 part
14	*Aja Mootra*				QS

Review of individual drugs of Bilwadi Agada is as follows:

1) *Bilwa (Mula)*

Rasa – Kashaya, Tikta (Mula: Madhura)
Guna – Laghu, Ruksha
Virya – Ushna Vipaka – Katu
***Doshaghnata*:** *Kaphavatashamaka*

Recent Research Articles: 1) The Hepatoprotective Effect of Bael Leaves (Aegle Marmelos) in Alcohol Induced Liver Injury in Albino Rats. [12]

2) Antioxidant and Phytochemical Properties of Aegle Marmelos Fruit Pulp.[13]

3) Review-Aegle Marmelos (Linn.) Correa: A potential source of Phytomedicine. [14]

2) *Surasa (Pushpa)*

Rasa – Katu, TiktaGuna – Laghu, Ruksha
Virya – UshnaVipaka – Katu
***Doshaghnata*:** *Kaphavatashashamaka*

Recent Research Articles: 1**)** Review Article the Science Behind Sacredness of Tulsi (Ocimum Sanctum Linn.). [15]

2) Hepatoprotective Activity of Ocimum Sanctum Leaf Extract Against Paracetamol Induced Hepatic Damage In Rats. [16]

3) *Karanja (Phala)*

Rasa – Tikta, Katu, KashayaGuna – Laghu, Tikshna
Virya – UshnaVipaka – Katu
***Doshaghnata**: Kaphavatashashamaka*

Recent Research Article: 1) A Review on Pongamia Pinnata (L) Pierre. A Great Versatile Leguminous Plant.[17]

4) *Nata*

Rasa – Tikta, Katu, KashayaGuna – Laghu, Snigdha
Virya – UshnaVipaka – Katu
***Doshaghnata:** Kaphavatashamaka*

5) *Surahwa*

Rasa – TiktaGuna – Laghu, Snigdha
Virya – UshnaVipaka – Katu
***Doshaghnata:** Kaphavatashamaka.*

Recent Research Article: 1) Herbs as liver savers- A review. [18]

2) Pharmacology of medicinal plants and natural products.[19]

6) *Haritaki (Phala)*

Rasa – Kashaya, Tikta, Madhura, Katu, AmlaGuna –Laghu, Ruksha
Virya – UshnaVipaka – Madhura
Prabhava - Tridoshashamaka
***Doshaghnata:** Tridoshashamaka, especially Vatashamaka.*

Recent Research: 1) Antihepatoprotective Potential of Livina, A Polyherbal Preparation On Paracetamol Induced Hepatotoxicity. [20]

2) Acetaminophen-Induced Hepato and Nephrotoxicity and Amelioration by Silymarin and Terminalia Chebula in Rats. [21]

7) *Bibhitaki (Phala*

Rasa – KashayaGuna –Ruksha, Laghu
Virya – UshnaVipaka – Madhura

Doshaghnata: *Tridoshashamaka, especially Kaphashamaka.*

Recent Research Articles:1) Antihepatoprotective Potential of Livina, A Polyherbal Preparation On Paracetamol Induced Hepatotoxicity. [20]

8) *Amalaki (Phala)*

Rasa – Amla, Madhura, Kashaya, Tikta, KatuGuna – Guru, Ruksha, Sheeta
Virya – Sheeta Vipaka – Madhura

Doshaghnata: *Tridoshashamaka, especially pittashamaka.*

Recent Research Articles:1) Roles of Emblica officinalis in Medicine A Review. [22]

2) Reversal of hepatotoxins-induced pre-fibrogenic events by Emblica officinalis – A histological study. [23]

9) *Shunthi*

Rasa – KatuGuna – Laghu, Snigdha
Virya – UshnaVipaka – Madhura

Doshaghnata: *vatakaphashamaka.*

Resent research Articles:1) Protective effects of *Zingiber officinale* (Zingiberaceae) against carbon tetrachloride and acetaminophen-induced hepatotoxicity in rats.[24]

2) *Zingiber officinale* Roscoe prevents acetaminophen-induced acute hepatotoxicity by enhancing hepatic antioxidant status. [25]

10) *Maricha*

Rasa – Katu Guna – Laghu, Tikshna, Ruksha
Virya – Ushna Vipaka – Katu

Doshaghnata: *Kaphavatashamaka*

Resent Research Articles:1) Protective role of Piperine against Cadmium induced hepatic and renal toxicity in mice. [26]

11) *Pippali*

Rasa – KatuGuna –Laghu, Snigdha, Tikshna
Virya – Anushna SheetaVipaka – Madhura

Doshaghnata: *Kaphavatashamaka.*

Recent Research Articles:1) Review Article on Chemistry and Pharmacology of Piper Longum. [27]

2) Recent studies on well-known spice. [28]

12) *Haridra*

Rasa – Tikta, KatuGuna – Ruksha, Laghu
Virya – UshnaVipaka – Katu

Doshaghnata: *Tridoshashamaka*

Recent Research Articles:1) Protective effect of Turmeric (*Curcuma longa*) in Paracetamol induced Hepatotoxicity in Rats. [29]

2) Review on Different Methods to Assess the Antioxidant Activity of Some Common Plants of Indian Traditional Medicine. [30]

13) *Daruharidra*

Rasa – Tikta, Kashaya (Rasanjana – katu)
Guna – Ruksha, Laghu
Virya – UshnaVipaka – Katu

Doshaghnata: *Kaphapittashashamaka.*

Recent Research Activity:1) Hepatoprotective Effects of Berberine On Carbon Tetrachloride-Induced Acute Hepatotoxicity in Rats. [31]

2) Antihepatoprotective Potential of Livina, A Polyherbal Preparation on Paracetamol Induced Hepatotoxicity - A Comparison with Silymarin. [20]

14) Goat's urine

Rasa – Katu, lavanaGuna – Laghu, Ruksha, Teekshna
Virya – Ushna Vipaka – Katu,

Doshaghnata: *Kapha Vaataghna*

Recent Research Article: 1) Animal products in traditional medicine from Attappady hills Western Ghats. [32]

DISCUSSION

As per classics *Bilwadi Agada* is indicated as ***Garavishahara***,[2]individual drugs having*Vishaghna, Shothaghna, Krumighna,*

Deepana, Pachana, Vranahara, Garanashaka, Bhutaghna and Yogavahi properties. Thus, *Bilwadi Agada* may act by virtue of its ***VishaghnaGuna***.

Literature reveals that, various ingredients of *Bilwadi Agada* having Antioxidant, immunomodulatory, Anti-inflammatory, Anti ulcerative & Hepatoprotective actions.[12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23] *Bilwadi Agada* may act by –

1. Prevent synthesis of prostaglandins, which may help as anti-inflammatory. 2. It may suppress CYP450, which play important role in producing toxic metabolite (NAPQI). 3. May be by increasing synthesis of Glutathione (GSH). 5. May help in regeneration and production of hepatocytes. Thus, above said actions of *Bilwadi Agada* may contribute towards its hepatoprotective activity.

CONCLUSION

Extensive research studies using models of experimental hepatic damage may help in establishing a definite rationale for the therapeutic use of Bilwadi Agada as a hepatoprotective drug in a laboratory setting and possibility of clinical studies should also be looked into.

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