



A Review on, Pharmacological and Biochemical Evaluation of Cardioprotective Activity of Aqueous Leaf Extract of *Abutilon Indicum* in Isoproterenol Induced Myocardial Infarction in Wistar Rats

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ABSTRACT

Cardiotoxicity is a condition that occurs during therapy with several cytotoxic drugs and may be the dose limiting factor in the cancer therapy or imbalanced diet and lifestyle. The use of herbal supplements has become increasingly popular in recent years. Among all the cardio vascular diseases, Myocardial infarction is considered as one of the most dangerous disease. The treatment available may not be sufficient to treat the disease as it is caused by many factors to overcome the adverse effects caused by the synthetic medicine available. There is a need for the natural therapy with the help of medicinal plants.

The term cardiovascular disease [CVD] is very much familiar which commonly refers to a group of diseases that affects heart and its parts, whereas the term CVD mostly refers to MI [Myocardial infarction], angina pectoris, hypertension, stroke and other circulatory diseases.

Keywords: CVD, MI

Introduction

Cardiotoxicity is a condition that occurs during therapy with several cytotoxic drugs and may be the dose limiting factor in the cancer therapy or imbalanced diet and lifestyle. The use of herbal supplements has become increasingly popular in recent years. Among all the cardio vascular diseases, Myocardial infarction is considered as one of the most dangerous disease. The treatment available may not be sufficient to treat the disease as it is caused by many factors to overcome the adverse effects caused by the synthetic medicine available. There is a need for the natural therapy with the help of medicinal plants.

Herbal medicine, also called botanical medicine or phytomedicine, refers to the use of seeds, berries, roots, leaves, bark, or flowers for medicinal purposes. Use of herbs and traditional systems of medicine is

becoming more main stream as improvements in analysis and quality control along with advances in clinical research show their value in the treatment and prevention of diseases.

From ancient time, plants have used as the major source of medicine and food for human being, and they have continued to provide mankind with new, novel therapeutic medicine and remedies. Since the last five decades, there has been a remarkably research in the study and use of herbal plants.

This current global interest in the study and use of medicinal plants has led to the characterization and identification of novel lead molecules, and isolation of active chemical compounds of therapeutic importance. The current world scenario of utilization of plant-derived natural remedies has created a dire need for accurate and up to date information on the characteristic

properties and therapeutic uses, efficacy, safety and quality of medicinal plant products.

The term cardiovascular disease [CVD] is very much familiar which commonly refers to a group of diseases that affects heart and its parts, whereas the term CVD mostly refers to MI [Myocardial infarction], angina pectoris, hypertension, stroke and other circulatory diseases. The common heart diseases that have been reported are coronary artery diseases, congestive heart failure, cardiac arrest, arrhythmias, and peripheral artery diseases.

It is known that number 1 cause of death globally is due to cardiovascular diseases because annually more people die from heart diseases than from any other grounds. Approximately 17.5 million people died from CVDs in the year 2012, representing 31% of all global deaths. Of these deaths, 7.4 million were due to coronary heart diseases and 6.7 million deaths were due to heart stroke.

Out of the 16 million deaths under the age of 60 due to non-communicable diseases, 85% are in low and middle income countries and 40% are caused by CVDs¹.

Cardiovascular diseases (CVDs).

Cardiovascular diseases (CVDs) are the most prevalent cause of death and disability worldwide. CVD, a group of disorders of the heart and the vasculature, includes high blood pressure, coronary heart disease, myocardial infarction, congestive heart failure, stroke and congenital heart defects.

Types of cardio vascular diseases [CVD]

There are different types of cardio vascular diseases among them based on the prevalence of diseases across the world the most considerable CVD are like Atherosclerosis, Myocardial infarction, Ischemia, Cardiomyopathy^{2,3}.

The medicinal plants are potential sources of drugs as they are rich in secondary metabolites and essential oils of therapeutic importance.

1. Uses of medicinal plants in various ailments are due to being economical, effective, their ease availability and due to their safety.

2. Because of these advantages the use of medicinal plants has been widely increased by the traditional medical practitioners in their day to day practice.
3. Foods are used commonly to meet our nutritional needs. However, foods obtained by plants contain a wide range of non-nutrient phytochemicals that are synthesized by plants for their own defence and for other biological functions. When we ingest these plant foods to meet our nutritional needs, we also ingest a wide variety of these non-nutrient phytochemicals. These phytochemicals have the potential for preventing chronic diseases and also non-toxic.
4. Cardiovascular disease is the number one cause of death globally and is projected to remain the leading cause of death. As many as 1.4 million children are suffering from heart related diseases in Pakistan and some 8,000 need heart surgeries annually, but out of them only 1,200 are operated upon. (Sixth "Biennial International Conference," organized by the Pakistan Society of Cardiovascular and Thoracic Surgeries). Free radicals play deleterious role to body established ischemia. Presence of various antioxidant compounds in fruits and vegetables, for example, vitamins C and E, b-carotene and polyphenolics have been associated with decreased risks of several chronic diseases, such as coronary heart disease and some cancers. Antioxidants scavenging the free radicals and protect the body. There is inverse relationship between intake of polyphenols and heart diseases.
5. There is a large and increasing global burden of cardiovascular disease. Approximately 14 million individuals died of cardiovascular disease in 1990, and this is projected to rise to about 25 million by 2020.
6. The global burden of disease due to cardiovascular diseases (CVDs) is escalating, principally due to a sharp rise in the developing countries which are experiencing rapid health transition.

7. The continuous increase in incidences of cardiovascular disease is a manifestation of chronic poor diet and lifestyle choices, which lead to diabetes and obesity.
8. More than 2000 plants have been listed in the Traditional (Herbal/Alternative) systems of medicine and some of these are providing comprehensive relief to the people suffering from cardio-vascular diseases, specially “hyperlipidemia” and “ischemic heart disease”. WHO reports indicate that around eighty percent of the global population still relies on botanical drugs and several herbal medicines have advanced to clinical use in modern times. The use of Western medicinal drugs for the treatment of hypertension, congestive heart failure and post myocardial infarction are widely accepted.
9. Various phytoconstituents from plants were responsible for cardioprotective activity.

Pharmacology of cardioprotective plants: Phytoconstituents reported in cardioprotective plants significantly prevented the altered biochemical variation such as marker enzymes serum glutamate- pyruvate transaminase (SGPT) or alanine transaminase (ALT), serum glutamate oxaloacetate transaminase (SGOT) or aspartate transaminase (AST), creatinephosphokinase (CPK), alkaline

phosphatase (ALP), lactate dehydrogenase (LDH), lipid profile including low density lipoprotein (LDL), VLDL (very low density lipoprotein), triglycerides (TGs), high density lipoprotein (HDL), total cholesterol and antioxidant parameters including Superoxide dismutase (SOD), glutathione (GSH), catalase (CAT), Glutathione peroxidase (GPx), MDA (malonaldehyde) and glutathione reductase (GR) come to near normal status. Cardioprotective activity was evaluated using various pharmacological screening models like isoprenaline induced myocardial necrosis in rats, doxorubicin (DOX) induced cardiotoxicity in albino rats, cyclophosphamide induced oxidative myocardial injury in a rat model, ischemia-reperfusion-induced myocardial infarction in albino rats, cigarette Smoke- exposed Rats, adriamycin-induced cardio Myopathy in rats etc.⁵⁻¹⁰

Abutilon indicum

Abutilon indicum (Indian abutilon, Indian mallow) is a small shrub in the family [Malvaceae](#), native to tropical and subtropical regions. This plant is a valuable medicinal and ornamental plant its roots and leaves being used for curing fevers. It has been widely introduced outside of its native range, and is considered invasive on certain tropical islands.¹³

Scientific classification

Kingdom:	Plantae
Clade:	Tracheophytes
Clade:	Angiosperms
Clade:	Eudicots
Clade:	Rosids
Order:	Malvales
Family:	Malvaceae
Genus:	Abutilon
Species:	<i>A. indicum</i>
<u>Binomial name</u>	
<i>Abutilon indicum</i>	
(Link) Sweet^[1]	



Abutilon indicum

Hindi name: "Kanghai"

- Urdu name: "Kanghi"
- Tamil name: "thuthi"
- Sanskrit name: अतिबला *Atibalaa*

Morphological characteristics of leaf:

leaves are simple, broadly ovate to deeply chordate, 7-9 nerved, serrate or crenate margins with alternate phyllotaxy. Upper surface of *Abutilon pannosum* leaf is somewhat scabrous while its lower surface is densely hairy or wooly in appearance. During rainy season leaf lamina of *Abutilon ramosum* reaches up to 20 centimeters in length with almost equal length of petioles.

Phytochemical Constituents:

Abutilon indicum contained many biological active chemical groups including, **cardenolides, steroids, tannins, glycosides, phenols, terpenoids, sugars, flavonoids, alkaloids and saponins.**

Phytochemical Investigations:

- ❖ Extraction of whole plant material
- ❖ Preliminary Phytochemical screening

Pharmacological Investigations:

A. In-Vitro

- ❖ Inhibition of calcium oxalate crystallization in human urine

❖ In-Vitro antioxidant activity:

1. DPPH Free radical scavenging activity
2. Phosphomolybdenum reduction assay
3. Nitric oxide radical-scavenging assay
4. Reducing power assay

B. In-Vivo

- ❖ Evaluation of Cardioprotective activity by Isoproterenol induced myocardial infarction
- ❖ Evaluation of Antioxidant potential of Cardioprotective activity by Isoproterenol induced myocardial infarction in wistar rats.
- ❖ **Histopathology of heart.**

MATERIALS AND METHODS³⁸⁻⁴¹

MATERIALS

Drugs –

- ❖ Ketamine hydrochloride injection (Aneket from Neon Laboratories Limited)
- ❖ Isoproterenol (Samarth Life Science Pvt Ltd)
- ❖ Verapamil (VPL from Samarth Life Science Pvt Ltd.)

Chemicals-

Table 1: List of chemicals

S.No.	List of Chemicals
1	Hydrogen peroxide (H ₂ O ₂)
2	5,5-Dithiobis 2-nitrobenzoic acid (DTNB)
3	Ether
4	Acetic acid
5	Thio barbituric acid
6	n-butanol pyridine
7	EDTA
8	Sucrose
9	Adrenaline
10	Trichloro acetic acid
11	Formalin
13	Potassium phosphate buffer
14	Sodium dodecyl sulphate
15	Ethanol
16	Sodium carbonate
17	Sodium hydroxide
20	Phosphate buffer
22	Formic acid
23	Hydrochloric acid
24	Sodium Nitroprusside
25	Chloroform
26	Sulphuric acid

Reagents will be prepared according to the need and some will be purchased from commercial sources.

Diagnostic kits: Diagnostic kits used for the estimation of marker enzymes CK-MB, LDH, SGOT and SGPT will be procured from **Span Diagnostic Ltd. India** and **AGAPPE Diagnostic. Instruments:**

- Micro centrifuge (“Microfuge” M/S Remi instruments Pvt. Ltd., Maharashtra, India).
- Semi Auto Analyser (MS 500 e, M/S Maysum technology Pvt. Ltd).
- ECG machine [Cardiart108DG (BPL)]
- Dhona balance (M/S Dhona instruments Pvt. Ltd., Kolkata, India)
- Colorimeter (Systronics, Photoelectric Colormeter-112)
- Tissue homogenizer (M/S Remi instruments Pvt. Ltd., Maharashtra, India)
- Autoclave

Result:

Reported Pharmacological Activity

Hepatoprotective Activity

- ❖ Porchezian E, *et al.* 2005 investigated Hepatoprotective activity of *Abution indicum* on experimental liver damage in rats.¹⁴
- ❖ Dash GK,. 2000 *et al* showed Hepatoprotective activity of leaves of *Abutilon indicum*¹⁵.
- ❖ Singh D *et al.* 2008 investigated Modulatory influence of *Abutolon indicum* leaves on Hepatic Antioxidant Status and Lipid Peroxidation against alcohol induced liver damage in Rats¹⁶.

Immunomodulatory Activity:

- ❖ Dashputre NL, *et al.* 2010. Investigated Immunomodulatory Activity of *Abutilon Indicum* Linn on Albino Mice¹⁷.

Anti-inflammatory and Analgesic activity:

- ❖ Saraswathi R, *et al.* 2011. Investigated phytochemical investigation, analgesic and anti-inflammatory activity of *Abutilon indicum* Linn¹⁸.
 - ❖ Parimaladevi B, *et al.* 2010. investigated evaluation of anti-inflammatory activity of methanol extract of *Abutilon indicum* and *Petalium murex*. A comparative study¹⁹.
 - ❖ Rajurkar R, *et al.* 2009. investigated Antiinflammatory Action of *Abutilon indicum* L. Sweet Leaves by HRBC Membrane Stabilization²⁰.
 - ❖ Bhajipale NS. *et al.* 2012 investigated evaluation of Anti-Arthritic Activity of Methanolic Extract of *Abutilon Indicum*²¹.
 - ❖ Tripathi PP, *et al.* 2012 investigated anti-Inflammatory Activity of *Abutilon Indicum* Extract²².
 - ❖ Ponnudurail K, *et al.* 2011. investigated evaluation of Anti-Inflammatory Activity of 75 Percent V/V Methanolic Extract of *Abutilon Indicum* Linn. Sweet Leaves²³.
 - ❖ Paranjape Archana N, *et al.* 2008 investigated Anti-inflammatory and Anti-asthmatic Activity *Abutilon indicum*²⁴.
 - ❖ Dsvdk K, *et al.* 2014. investigated evaluation of anti-inflammatory and anti-proliferative activity of *Abutilon indicum*²⁵.
 - ❖ Kushwaha SK, *et al.* 2014 investigated Antinociceptive and Anti-inflammatory activities of Quercetin isolated from ethanolic extract of *Abutilon indicum* L²⁶.
 - ❖ Ahmed M, *et al.* 2000. investigated analgesic principle from *Abutilon indicum*²⁷.
 - ❖ Goyal N, *et al.* 2009 investigated Analgesic effects of various extracts of the root of *Abutilon indicum* Linn²⁸.
 - ❖ Deshpande V, *et al.* 2009 investigated *In-vitro* anti-arthritic activity of *Abutilon indicum* (Linn.) Sweet²⁹.
- Antiulcer Activity:**
- ❖ Malgi RA, *et al.* 2009 investigated antiulcer activity of *Abutilon indicum* L. sweet, leaf extract using different experimental models³⁰.
 - ❖ Dashputre NL, *et al.* 2010. investigated evaluation of Anti-Ulcer Activity of Methanolic Extract of *Abutilon indicum* Linn Leaves in Experimental Rats³¹.
- Antioxidant Activity:**
- ❖ Kaushik D, *et al.* 2010. investigated evaluation of antioxidant and antimicrobial activity of *Abutilon indicum*³².
 - ❖ Khokra SL. *et al.* 2011 investigated *in vivo* antioxidant activity of plant *Abutilon indicum*³³.
 - ❖ Srikanth PP, *et al.* 2012. investigated evaluation of Antioxidant and Anticancer Properties of Methanolic Extracts of *Abutilon indicum* and *Blumea mollis*³⁴.
 - ❖ Yasmin S, *et al.* 2010. investigated Antioxidant potential and radical scavenging effects of various extracts from *Abutilon indicum* and *Abutilon muticum*³⁵.
 - ❖ Chakraborty GS *et al.* 2009 investigated antioxidant activity of *Abutilon indicum* leaves³⁶.
 - ❖ Sowjanya KR, *et al.* 2012 investigated *In vitro* antioxidant activity of ultra-sonic bath assisted ethanol extract of *Abutilon indicum* leaf³⁷.
 - ❖ Ahmad J, *et al.* 2012. investigated antioxidant potential of *Abutilon indicum* (L.)³⁸.
 - ❖ Mrinmoy GS, *et al.* 2011 investigated evaluating the antioxidant activities in the leaf extract of a medicinal plant, *Abutilon indicum* (linn.) Sweet³⁹.
 - ❖ Chakraborty GS, *et al.* 2010. investigated free radical scavenging activity of *Abutilon indicum* (Linn) sweet stem extracts⁴⁰.
 - ❖ Kalyani B. *et al.* 2011 investigated Hepatoprotective and antioxidant role of flower extract of *Abutilon indicum*⁴¹.
 - ❖ Sammia Y, *et al.* 2010 investigated antioxidant potential and radical scavenging effects of various extracts from *Abutilon indicum* and *Abutilon muticum*⁴².
- Cardioprotective activity:**
- ❖ Amaranth KR, *et al.* 2008 investigated Cardioprotective activity of ethanolic root extract of *Abutilon indicum* in isoproterenol induced myocardial infarction in male wistar rats⁴³.

Anticonvulsant activity:

- ❖ Golwala DK, *et al.* 2010 investigated anticonvulsant activity of *Abutilon indicum* leaf⁴⁴.

Antihyperlipidemic activity:

- ❖ Srividya AR, *et al.* 2011 investigated Phytopreventive and antihyperlipidemic activity of *Abutilon indicum* leaves⁴⁵.

Antimicrobial Activity:

- ❖ Poonkothai M. *et al.* 2006 investigated antibacterial Activity of Leaf Extract of *Abutilon indicum*⁴⁶.
- ❖ Muhit A, *et al.* 2010 investigated Cytotoxic and Antimicrobial Activity of the Crede Extract of *Abutilon indicum*⁴⁷.
- ❖ Mateen A, *et al.* 2011 investigated evaluation of antibacterial activity of *Cuscuta reflexa* and *Abutilon indicum*⁴⁸.
- ❖ Lokesh R, *et al.* 2016 investigated antibacterial and antioxidant activity of saponin from *Abutilon indicum* leaves⁴⁹.
- ❖ Prabhuji S.K, *et al.* 2010 investigated Antifungal activity of a new steroid isolated from *Abutilon indicum* (L.)⁵⁰.
- ❖ Padma R., *et al.* 2009 investigated Antimycotic activity of the components of *Abutilon indicum*⁵¹.

Anthelmintic Activity:

- ❖ Chumbhale D, *et al.* 2013 investigated in-vitro anthelmintic activity of *Abutilon indicum* (L.) Sweet and *Abelmoschus manihot* L. medic⁵².

Antidiarrheal activity:

- ❖ Chandrashekhar VM, *et al.* 2000 investigated anti-diarrhoeal activity of *Abutilon indicum* Linn. Leaf extract⁵³.

Wound healing activity

- Roshan S, *et al.* 2008 investigated Wound healing activity of *Abutilon indicum*⁵⁴.

Diuretic Activity:

- ❖ Balamurugan G, *et al.* 2010 investigated diuretic Activity of *Abutilon Indicum* Linn (Sweet) Seed Extract⁵⁵.

Antidiabetic activity:

- ❖ Seetharam YN, *et al.* 2002 investigated Hypoglycemic activity of *Abutilon indicum* leaf extracts in rats⁵⁶.
- ❖ Kaushik P, *et al.* 2012 investigated antidiabetic activity of plant *Abutilon*

indicum in streptozotocin-induced experimental diabetes in rats⁵⁷

Keywords

- ❖ Cardiovascular
- ❖ Phytochemicals
- ❖ Isoproterenol

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