REVIEW ON ROLE OF AYURVEDA IN THROMBOSIS - A MAJOR CAUSE OF CARDIOVASCULAR DISEASES
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ABSTRACT
A cardiovascular disease (CVD) is the world’s largest cause of death, claiming 17.1 million lives a year. Thrombosis is the widespread cause of CVD. Rudolph Virchow discovered three factors for thrombus formation known as Virchow’s triad. Modern medicine is capable to deal with it in curative aspect, but is found to be lacking in prevention. So this review was made to explore the Ayurveda literature & related research to come out with some result in curative as well as preventive aspect. In Ayurveda, the term ‘Dhamanipratichaya’ described under Kaphaja Nanatmajavikara. Some herbs are illustrated under the name of specific action such as lekhan(having scrapping action), chedan(scarificient) etc. Some studies proved vasodilator effect of snehan(massage therapy) and swedan(Thermotherapy). It also increases the supply of oxygen and nutrients and the elimination of carbon dioxide and metabolic waste. Animal studies showed significant efficacy of some herbs as a thrombolytic agent. It is concluded that many treatment modalities and herbs are described in Ayurveda which may perhaps be helpful to treat or prevent thrombosis but still a very less amount of research work is done in this regard. So there is a huge scope of research to assess these modalities on modern parameters.

Key words - Virchow’s triad, thrombosis, Anti-platelet, Dhamanipratichaya, Lekhana, Chedana

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INTRODUCTION:
Cardiovascular diseases (CVD), including myocardial infarction and stroke is the world’s largest cause of death, claiming 17.1 million lives a year\[^1\]. Thrombosis is the commonest cause of CVD in developed countries and is a growing endemic in developing countries because of increasing prevalence of smoking, obesity, hypertension and type 2 diabetes.

Haemostasis is an essential mechanism of body, but the pathological formation of a thrombus causes significant health risks. German pathologist Rudolph Virchow discovered three factors for thrombus formation known as Virchow’s triad. These factors are Blood stasis, Endothelial Damage & Hypercoagulability\[^2\]. One or more of these factors causes arterial or venous thrombus. Arterial and venous thrombi differ in composition and appearance. Arterial thrombi are typically composed mainly of platelet aggregates, giving the appearance of ‘white thrombi’. Venous thrombi mostly consist of fibrin and red blood cells so are known as ‘red thrombi’.

Venous thrombosis is supposed to begin at the venous valves\[^3\]. These valves play a major role in blood circulation in the legs. They are also areas where stasis and hypoxia may occur. Direct evidence from autopsy studies and phlebography has recognized the venous valvular sinus is a frequent location of thrombosis initiation\[^4\]. This phenomenon has been attributed to stasis of blood which is the components of Virchow’s triad. The blood clots detach from the vascular wall and travel in the blood called as emboli. It can lodge anywhere in the cardiovascular system. Increased levels of coagulation factors, particularly factor VIII, Von Willebrand factor, factor VII and prothrombin are also associated with an increased risk of thrombosis\[^5,6\]. It is also found that the risk of thrombosis is increases with aging. The basis of it remains uncertain. Increase in body mass with age\[^7\] and immobilization due to illness\[^8\] might be the contributing factors. Post operative thrombosis is a complication of especially knee, hip and cancer surgery. In the case of knee and hip surgery, damage to the veins in combination with stasis is thought to be major contributing factors\[^9\]. In addition, materials released from the surgical sites into the blood stream can increase the risk of coagulation. Cancer surgeries contribute to thrombosis due to the release of tumor procoagulants, host inflammatory responses and responses to chemotherapeutics\[^10\].

Need of review: Thrombosis is a leading cause of cardio-vascular diseases. Hence, anticoagulation therapy plays a vital role in the prevention and treatment of thrombo-embolic disorders\[^11\]. For more than five decades, anticoagulant drugs are frequently used but
the life-threatening side effects of these drugs have also been well documented\textsuperscript{[12]}. So this review was made to explore the Ayurveda literature & related research articles which will be helpful to come out with some result in curative as well as preventive aspect.

**Thrombosis in Ayurveda perspective**– There is no directly resembling term for thrombosis but the term ‘Dhamanipratichaya’ described under Kaphaja Nanatmajavikara can be correlated with atherosclerosis\textsuperscript{[13]}. It is caused due to accumulation of *kapha* (biological humor) and *meda* (fatty tissue) in the blood. This excess accumulation of the *kapha* and *meda* in blood is called as *shonitabhishyandan* (thickness of blood). This accumulated *kapha* and *meda* adhere to *dhamani* causes narrowing and lack of distensibility of *dhamani*. *Shonitabhishyandan* may also leads to *sirajagranthi* (glandular structure in vessels)\textsuperscript{[14]}. In charaksamhita ‘Dhamani sankoch’ Gambhira Vatarakta\textsuperscript{[15]}. It is not directly related to thrombosis but can be correlated with Vasospasm.

In Ayurveda literature, some drugs are illustrated under the name of specific *karma* (pharmacological action) such as *lekhan* (having scrapping property), *chedan* (scarificient), *pramathi* (Decongestant)& *vayasthapam* (Longevity provider).

*Lekhan* drugs scrap unwanted tissues & metabolic waste from the body. *Vacha* (*Acorus calamus*), *Yava* (*barley*), *Koshna jala* (*luke warm water*) & *kshaudra* (*honey*) are described as best *lekhan dravya*\textsuperscript{[16]}. Dalhan has characterized the *lekhana drug* is the one which is having properties of *Vata* (one of biological humor) and *Agni* (Digestive fire)\textsuperscript{[17]}.

No study was found on *Vacha* and *Yava* to assess its *lekhana* property on modern parameters. The previous studies carried out on honey found a wide range of phenolic compounds which showed potential effect in cardiovascular diseases. In coronary heart disease (CHD), the protective effects of phenolic compounds include antithrombotic and vasorelaxant\textsuperscript{[18]}. So honey can be helpful in preventing thrombosis and vasospasm.

The drug which forcefully detaches the deeply attached *mala* (metabolic waste) & *dosha* (vitiated biological humor) are called as *chedan dravya*. *Kshar, Marich* & *shilajatu* are described as *chedan dravya*\textsuperscript{[19]}. *Pramathi* are the drugs which expel the mala from various channels. *Marich* (*piper nigrum*) and *Vacha* (*Acorus calamus*) are known as *pramathi* drugs\textsuperscript{[20]}.

*Marich, kshara* & *shilajatu* are frequently used in practice for different ailments but are not used in thrombo-embolic disorders. It might be due to lack of clinical research in this area.
Vayasthapan drugs prevent the ageing process. Charak described Amalaki as a best vayasthapan drug. As aging is found the causative factor of thrombosis formation; it can be used to prevent thrombosis. In many studies, Amalaki (Embelica officinalis) found to protect endothelial function. Laboratory studies using cultured endothelial cells and experimental models show that treatment with Amalaki extract enhances production of nitric oxide, the signaling molecule useful to relax and maintain normal blood flow[21, 22, 23].

Blood stasis is an important cause of thrombosis. It can be prevented by Snehan chikitsa (Massage therapy) which is frequently used by Ayurveda practitioners. Massage is commonly seen as a therapeutic art without scientific foundation. Some studies found that Massage dilates superficial blood vessels and increases the rate of blood flow. Deep massage promotes venous return and increases cardiac stroke volume [24, 25]. Thrombosis frequently results from poor venous return [26] and can be prevented by massage. Bed ridden patients are particularly at risk of venous stasis. In the study of Sabri S et al, Massage given unilaterally decreased the incidence of deep venous thrombosis (DVT) in the treated limb by 82% compared with that in the untreated leg [27]. In other study of Ernst E et al, 20 minutes whole body massage decreased both blood viscosity and haematocrit, indicating haemodilution [28].

The vascular endothelium, which regulates the passage of macromolecules and circulating cells from blood to tissues, is a major target of oxidative stress, playing a critical role in the pathophysiology of several vascular diseases and disorders [29]. Endothelial dysfunction is a reversible disorder, and strategies can be aimed to cure & prevent it.

Swedan (Thermotherapy) is the therapeutic application of any substance to the body that adds heat to the body resulting in increased tissue temperature. Swedan is typically indicated for vata and kapha dosha. It increases blood volume, oxygenation, and nutrition. It also increases white blood cells, stimulating an immune system response. Heat creates higher tissue temperatures, which produces vasodilatation that increases the supply of oxygen and nutrients and the elimination of carbon dioxide and metabolic waste [30].

Thermotherapy is delivered by three mechanisms: conduction, convection or conversion. Increased blood flow facilitates tissue healing by supplying protein, nutrients, and oxygen at the site of injury. A 1ºC increase in tissue temperature is associated with a 10% to 15% increase in local tissue metabolism [31]. This increase in metabolism aids the healing process by increasing both catabolic and
anabolic reactions needed to degrade and remove metabolic by-products of tissue damage and provides the milieu for tissue repair.

Post operative thrombosis is a complication of especially knee, hip and cancer surgery. In considering above mechanism of action, snehan and swedan can be helpful to prevent this complication.

Hypercoagulability is the other factor to cause thrombosis. It occurs if the normal balance of the clotting system is upset. In Charak Samhita, Katu rasa (Pungent taste) is ascribed with the property of ‘shonitasanghatabhedana’ (thrombolysis)\(^{[32]}\). Acharya Sushruta has described following drugs which facilitates the free flow of blood in Shonitavarnaniya adhyaya. Ela (Elettaria cardamomum), Karpoora (Cinnamomum camphora), Kushta (Saussurea lappa), Tagara (Valeriana wallichii), Patha (Cissampelos pariera), Bhadrararu (Cedrus deodara), Vidanga (Embelia ribes), Chitraka (Plumbago zeylanica), Trikatu (Piper longum, Piper nigrum, Zingiber officinale), Agaradhma, Haridra (Curcuma longa) and Naktamalaphala (Pongamia pinnata)\(^{[33]}\).

In-vitro research of above some drugs & the other drugs which are not described especially under the group of lekhan,chedan are also found to be having significant Antithrombotic property.

- **Haridra (Curcuma longa)** – In the study conducted by Lee HS, active constituent of the rhizome of Curcuma longa was isolated and it was found as more potent platelet inhibitor in comparison with aspirin\(^{[34]}\).

- **Pippali (Piper longum)** - S Park et al conducted an animal study. They isolated four acidamides (piperine, pipernonaline, piperoctadecalidine,and piperlongumine) from its fruits which showed inhibitory activities on washed rabbit platelet aggregation induced by collagen, arachidonic acid (AA), and platelet-activating factor (PAF)\(^{[35]}\).

- **Harithaki (Terminalia chebula)** - Acharya Sushruta has described Haritaki as the best drug for santarpanjanya vikar( diseases due to impaired fat metabolism)\(^{[36]}\). The methanolic extracts of its fruits exhibited potent platelet aggregation inhibition activity in a dose-dependent manner at concentration range (1 to 10 mg/ml)\(^{[37]}\).

- **Kumbhi (Careya arborea)** – It is an important medicinal plant. The methanolic bark extract of it exhibited anticoagulant activities when compared with the standard warfarin. It prolonged the time taken for blood clotting and there was a significant increase in the activated Partial Thromboplastin Time, Prothrombin Time and Thrombin Time\(^{[38]}\).
• **Manjishtha (Rubia cordifolia)** - It is commonly used as a Raktaprasadak (blood purifier). It was studied on rabbit platelets and it was found to be effective in inhibiting the platelet aggregation induced by PAF (platelet activating factor)\(^{[39]}\).

• **Vidarikanda (Pueraria tuberosa)** – It is commonly known for its Bruhan (restorative) & Rasayan (Rejuvanative) property\(^{[40]}\). In a study by Yu Z et al found that Puerariae isoflavone in the dose of 500, 1000 mg/kg% x 7 days per oral has significantly lowered blood viscosity and platelet adhesion rate, inhibited thrombosis and ADP-induced platelet aggregation in rats, and showed obvious antagonism for platelet thrombosis in ADP-treated mice\(^{[41]}\).

• **Kalmegh (Andrographis paniculata)** – It is commonly used in the management of jaundice & other liver disorders. It is found to be effective in inhibiting platelet-activating factor (PAF)-induced platelet aggregation in a dose-dependent manner\(^{[42]}\).

• **Guggulu (Commiphora wightii)** – It is known as deepana (digestive fire enhancer), medohara (fat reducer) and rasayana (Rejuvanator)\(^{[43]}\). The Guggulsterones present in it has platelet antiaggregant activity by completely inhibiting Platelet aggregation induced by adenosine diphosphate, adrenaline or serotonin\(^{[44]}\).

• **Ardrak (Zingiber officinale)** - In a study some of the isolates from Z.officinale i.e. [6]- gingerol and [6]-shogaol were evaluated for their antiplatelet aggregation and vasorelaxing bioactivities and found to be potent anti-platelet aggregation bioactivity\(^{[45]}\).

These herbs can be used as preventive & curative purpose in disorders related to thrombosis.

**CONCLUSION**: From this review, it is observed that thrombosis is a prime cause of cardiovascular diseases. Ayurveda has a numerous description associated to thrombosis. Despite its wide spread usage these medicines have not been evaluated scientifically with regard to their safety and efficacy. The drugs which are specifically having lekhan, chedan or pramathi property are still neglected in research. The procedures like snehan & swedan need to explore for its role in thrombotic disorders so there is an imperative need to look for research in this field.

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