

Removal Of Toxicity in Traditional Iron Based Herbo-Metallic Preparations – A Scientific Perspective

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ABSTRACT

Herbometallic preparations are unique formulations that could be used in very minimal doses to treat various diseases and disorders. Even now, Ayurveda and Siddha practitioners use such herbo-metallic formulations more, owing to their quick action and small dosage as compared to herbal preparations. Various metals such as iron, gold, silver, copper, zinc, tin, lead, etc., are being used to prepare herbo-mineral formulations. The starting metal undergoes various steps of detoxification process involving treatment with plant powders and decoctions and a calcination process where the hard metal is transformed into a fine nano powder. This transformation is made possible only because of possible interactions between the phytoingredients and the metals. When iron is used as a raw material in the preparation of Indian traditional drugs, it is always treated with herbs such as *Oryza sativa* (seeds), *Macrotyloma uniflorum* (seeds), *Terminalia chebula* (fruit), *Terminalia bellerica* (fruit), *Phyllanthus emblica* (fruit), *Tamarindus indica* (leaf), *Wedelia chinensis* (leaf), *Citrus lemon* (fruit), and *Aloe vera* (leaf) that have been used for detoxification, reduction and stabilization of iron. In this study, an attempt has been made to review the scientific perspectives of detoxification of iron used in Indian herbo-metallic preparations and unravel the science involved in this process.

Keywords: Iron, Indian systems of medicine, Herbo-metallic, Detoxification.

INTRODUCTION

Ayurveda and *Siddha* are two major traditional medicines of India, contributing significantly to the healthcare of mankind since time immemorial. *Ayurveda* is widely considered to be a holistic medicinal system recommended for human health care. *Siddha* is another ancient traditional system of India, developed by *Siddhars* or masters who attained perfection in all aspects including health. In both the systems, plants find major use in the preparation or purification of metallic/mineral preparations.

Herbometallic preparations are unique formulations that could be used in very minimal doses to treat various diseases and disorders. In *Ayurveda*, a *Bhasma* obtained after repeated incineration of herbal decoctions is believed to be devoid of the toxic effects of the metals but are also regarded as nanoparticles due to their resemblance of physico-chemical

properties to nanocrystalline materials¹. In *Charaka Samhita*, mention has been made about the usage of nanometal particles. Various metals such as iron, gold, silver, copper, zinc, tin, lead, etc., are being used to prepare herbo-mineral formulations². These metal nano particles are unique and safe and reported to have excellent biological activities including management of SARS-COV-2³.

In the present review, iron based metallic preparations are selected and reviewed from the point of view of iron interactions with herbs, herbal extracts and molecules.

Methodology

The present study was initiated with an extensive literature review on iron-based *Ayurveda* and *Siddha* formulations, purification and detoxification methods, role of herbal ingredients in iron purification and transformation conducted in accordance with

Relevant conflicts of interest/financial disclosures: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

PRISMA guidelines. Research articles published between 2004-2022 were identified through survey of scholarly articles in Science direct, Scopus, PubMed and Google Scholar. Some articles were also selected from the reference section of the selected research articles.

Iron-based preparations

Iron is widely used to prepare traditional medicines in both Indian and Chinese systems of medicines⁴. It is used in Ayurvedic preparations like *Lauha* bhasma,

Teekshnalauha bhasma, Mandura bhasma and Kantha bhasma. In Siddha system of medicine, iron is used to prepare various herbo-mineral formulations like Annabethi chenduram, Aya chenduram, Ayakantha chenduram, Mandura chenduram, Mandura mathirai, Manduraadai kasayam, Ayabringaraja karpam, Ayaveera chenduram, Arumuga chenduram, Kandha chenduram, Kantha parpam, Aya melugu and Ayasambeerakarpam (Table 1a, 1b, 2).

Table 1a. Iron based formulations of the Ayurvedic system selected for review

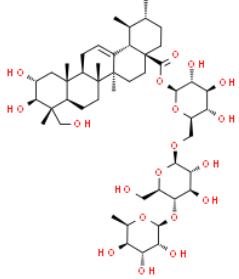
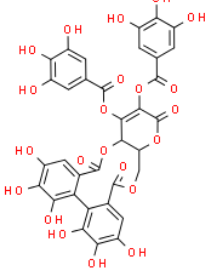
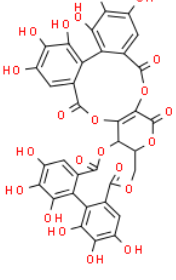
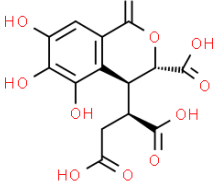
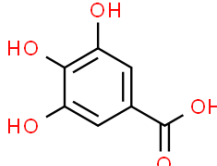
S.No	Name of the iron-based formulation	Therapeutic applications
1.	Lauha bhasma	Anaemia, Jaundice ⁵
2.	Teekshnalauha bhasma	Diarrhoea and Diabetes ⁶
3.	Mandura bhasma	Jaundice and Oedema ⁵
4.	Pippalyadi lauha	Nasal congestion and dyspnoea ⁵

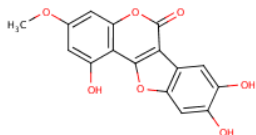
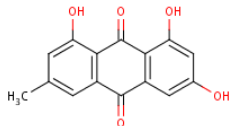
Table 1b. Iron based formulations of the Siddha system selected for review

S.No	Name of the iron-based formulation	Therapeutic applications
1.	Annabethichenduram	Helps in digestion and acts as an antioxidant ⁷
2.	Aya parpam	Useful in treating inflammation and diabetes conditions ⁸
3.	Ayakanthachenduram	All types of anaemia ⁹
4.	Mandurachenduram	Jaundice and oedema ⁷
5.	Manduramathirai	Anaemia, Jaundice ⁸
6.	Manduraadaikasayam	Hepatomegaly and splenomegaly ⁸
7.	Ayabringarajakarpam	Anaemia and swelling ²
8.	Ayaveerachenduram	Body pain and act as a antidote ²
9.	Arumugachenduram	Joint pain and head ache ⁸
10.	Kandhachenduram	Hepatomegaly and splenomegaly (Thiagarajan, 2004)
11.	Kantha parpam	Respiratory tract diseases ²
12.	Aya melugu	Anaemia, Jaundice ²
13.	Ayasambeerakarpam	Anaemia, Jaundice ²
14.	Ayanagaparpam	Chronic diseases like wheezing, asthma and tuberculosis ²



Table 2. Significance of traditional plants as ingredients and their contribution in the purification processes of Herbo metallic preparation

Scientific Name of Herbal ingredient	Main phytocompound of the plant	Structure	Iron interactions with purifying/ingredient plants and the therapeutic role of the phytoingredient
Centella asiatica (L.) Urb.	Asiaticoside		In the Kantha parpam ² where magnetite is used, components of Centella asiatica contributes as a chelator in complex formation and in improving antioxidant status.
Emblica officinalis Gaertn	Emblicanin A		In the Aya centuram Lauhabhasma ⁷ where impure iron is used, components of Emblica officinalis contributes as a chelator in complex formation. Enhances hepatoprotection and acts as an immunomodulatory agent in fighting against diseases and disorders.
	Emblicanin B		
Terminalia chebula Retz.)	Chebolic acid		In the Kantha Chenduram (where magnetite is used) and Punarnavadi mandura ² where dross iron is used, components of Terminalia chebula contributes as a chelator in complex formation
Terminalia bellerica (Gaertn.) Roxb	Gallic acid		In the Lauha bhasma ² where impure iron is used, treatment with gallic acid containing fruits enhances antidiabetic and antioxidant potential

Eclipta alba (L.)	Wedelolactone		In the Aya centuram Ayakantha centuram ⁹ where iron fillings are used, the components of <i>Eclipta alba</i> contributes as a chelator in complex formation. Enhances hepatoprotective activity and normal liver function and helps in preventing anaemic conditions.
Aloe vera (L.) Burm.f.	Emodin		In the Aya parpam ² , where iron fillings are used, the components of Aloe vera contributes as a chelator in complex formation. Enhances therapeutic potential such as anti-inflammatory and antidiabetic

For the preparation of iron-based formulations, iron is collected from nature in impure form and purified and detoxified by various treatment methods employing plants and plant juices such as rice gruel (*Oryza sativa*), horse gram (*Macrotyloma uniflorum*) extract, Triphalakasaya, *Wedelia chinensis*, Citrus limon, *Tamarindus indica*, *Mollugolotoides*, *Musa paradisiaca*, *Limoniaacidissima*, *Moringa oleifera* depending upon the nature of different iron-based preparations.

Detoxification of Iron

The starting metal used in herbo-metallic formulations is subjected to detoxification process to make the metallic drugs biocompatible and converting into a specific chemical form. This detoxification process of metals contains 2 steps – Step 1. Purification (*Shodhana*) and Step 2. Calcination (*Maarana*). Due to these purification and calcinations processes, considerable reduction in the particle size of the metals and metallic compounds as well change in the structure of the metal is also obtained, which converts the toxic metal into a non-toxic form. It is interesting to note that each metal is processed with specific herbs which make the metal to undergo changes during the step of grinding (*Bhavana*), heating (*Svedhana*), immersing (*Nirvavana*) and triturating (*Mardhana*). In this

purification process, one is a common method (*Saamanya shodhana*) for all the metals but the second is a special method (*Visesha shodhana*), where only specific herbs are used for specific metals.

Impact of Herbal agents used in Common methods of Iron purification

Rice gruel

After treating the hard blackish iron with gingely oil, curd and cow's urine, it is treated with rice gruel. This treatment transforms the hard iron metal into coloured lusterless, brittle powder. *Lauhabhasma* (iron ash) is an iron-based herbo-metallic preparation that has several therapeutic applications¹⁰. In the preparation of *Lauha bhasma*, red-hot iron is treated sequentially with sesame oil, butter milk, cow's urine, rice gruel and horse gram decoction and in a special purification process, the treated iron is further purified using herbal extracts¹¹ (Gupta et al. 2012). Krishnamachary et al. (2012)¹² observed that use of rice-gruel removes Fe³⁺ through formation of coordination compounds. Rice gruel contains about 0.93% protein, 0.41% liquid, 0.27% ash and 8.66% of carbohydrate. It is also reported that rice gruel components could transport dioxygen under aerobic condition and oxidizes Fe (II) to Fe (III) hydroxide, and thus chelates the excess amount of iron¹³. Preparation of Teekshnalauha bhasma was standardized by Rakesh



Singh et al. (2016)¹⁴ using rice gruel. At the end of purification with rice gruel, the lustrous and rigid form of iron was converted into a black colored lusterless powder of brittle material. Treatment with rice gruel facilitates elimination of inorganic impurities while introducing beneficial organic components into the iron¹⁵.

Macrotyloma uniflorum extract in the chemical transformation of Iron

Phytoingredients of *Macrotyloma uniflorum* include Gallic acid, P-coumaric acid, P-Hydroxy benzoic acid

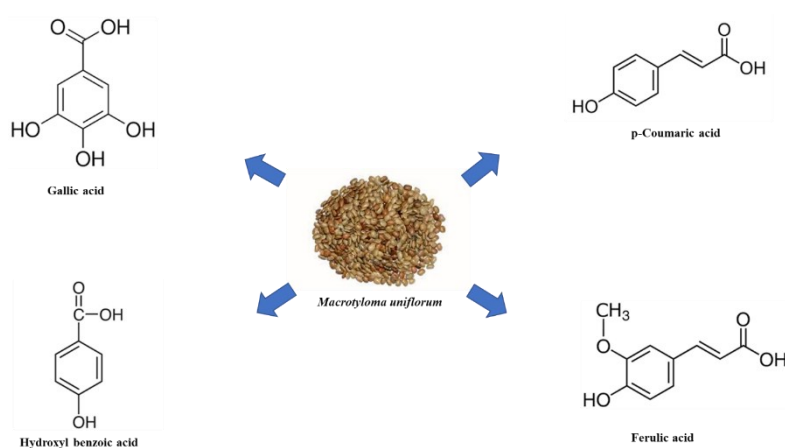


Figure 1. Major phytochemicals in Horse gram (*Macrotyloma uniflorum*) decoction used in iron purification

In our earlier paper¹⁸, the data obtained demonstrated that gallic acid readily formed a complex with iron (III) chloride through the phenolic groups; the carboxylic acid group of gallic acid was not involved in the coordination with the metal ion. In this study the authors evaluated the role of gallic acid in the purification process and they have demonstrated that gallic acid, which has one -CO₂H and three phenolic groups, coordinates with iron through the two phenolic groups giving rise to an octahedral complex with D₃ symmetry. The thermal analysis showed that the complex was stable up to 850°C and the complex formed was soluble in water.

Thus, gallic acid present in *Macrotyloma uniflorum* extract is believed to be responsible in removing Fe (III) present in the raw material thereby reducing the toxicity of *Lauha bhasma*. Further, the gallic acid-

and ferulic acid^{12, 16}. In an intermediate step of *Lauhabhasma* preparation, iron was heated to a red-hot form and immersed in horse gram (*Macrotyloma uniflorum*) decoction, which contains gallic acid (**Figure 1**) that forms water soluble complexes with Fe³⁺¹⁷. Hence, the authors noted that the removal of any remaining Fe³⁺ can be attained through treatment with horse gram decoction. Further, polyphenols with di- and trihydroxy benzene ring in *Macrotyloma uniflorum* extract may be involved in the transition of iron from its oxidized state to reduced state¹³.

metal complex was soluble in water and thus the treatment of iron with *Macrotyloma uniflorum* extract resulted in the formation of water-soluble complex, which was removed during repeated washing. Thus, we established for the first time, the scientific basis of using *Macrotyloma uniflorum* extract in the purification of iron and demonstrated that, during this process, the trivalent iron, which was present in the raw material, was removed, thereby reducing the iron (III) content in the iron based Ayurvedic preparation *Lauha bhasma*.

Decoction of *Macrotyloma uniflorum* is also used to prepare Teekshna lauha bhasma¹⁴. Authors suggested that the oxide layers developed as a result of the raw material's exposure to atmospheric oxidation were removed by treatment with *Macrotyloma uniflorum* extract decoction. Geetha Sudheer et al. (2015)¹⁷

prepared Kantha chenturam and the raw material was purified using horse gram (*Macrotyloma uniflorum*) decoction. Kantha chenturam is an iron-oxide based formulation commonly used to treat conditions such as infections, rheumatologic diseases, hepatic and respiratory disorders, and allergies in Siddha system of medicine. Based on characterization studies using XRF, FTIR, TGA and XRD, it was identified that the herbal extracts helped to convert the raw kantham (iron oxide) into *kantha* chenturam. Chemically, the alpha-quartz was transformed into a surface coat of silicate on the iron oxide by the herbal extracts and there was no organo-metall complex found in the final product.

Impact of Herbal agents used in Special/Specific methods of Iron purification

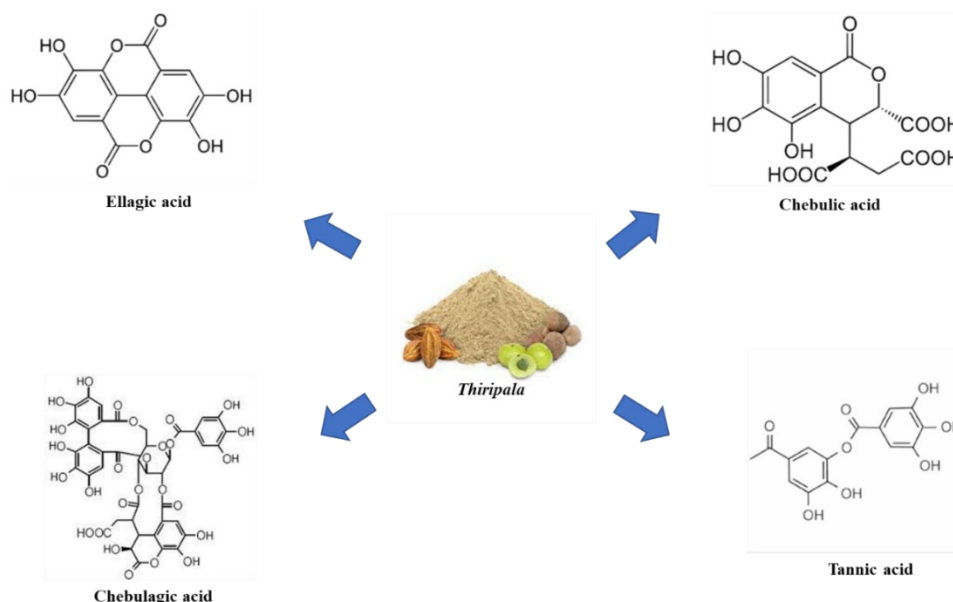


Figure 2. Major phytochemicals in Triphala (*Terminalia chebula*, *Terminalia bellerica* and *Phyllanthus emblica*) decoction used in iron purification

Any Fe^{3+} present in the sample was expected to form a water-soluble complex with gallic acid and was removed in the supernatant solution. The authors concluded that the use of plant extracts facilitated the removal of Fe^{3+} present in the raw material by forming a soluble complex and also resulted in the retention of Fe^{2+} by forming an insoluble complex. In another study, Krishnamachary et al. (2014)²⁵ observed that the use of *Triphala* aqueous extract increased the temperature during calcination process of *Lauha bhasma*, which helped in the conversion of Fe_3O_4 and

Triphala kasaya

In the special method of Lauha bhasma preparation, Triphala kasaya (decoction of *Terminalia chebula*, *Terminalia bellerica* and *Phyllanthus emblica* fruits) was added to iron after special purification and was allowed to dry under sun¹². The authors claimed that the reaction between the herbal constituents¹⁹⁻²⁴ and iron may be responsible for maintaining the Fe^{2+} form without getting oxidized. The sample originally in the form of a homogenous liquid, turned into a suspension of solid particles after these steps. The solid particles were recognized as water-insoluble complexes of Fe^{2+} with gallic acid and tannic acid, which were present in decoction of Triphala (**Figure 2**).

gamma (γ)- Fe_2O_3 to alpha (α)- Fe_2O_3 which is the biocompatible form of iron.

Teekshnalauha bhasma was treated seven times with *Triphala kwatha* (Decoction of *Terminalia chebula*, *Terminalia bellirica* and *Phyllanthus emblica* fruits) under *vishesha shodhana*¹⁴. After the process of *vishesha shodhana*, the brittleness and weight of *Teekshna lauha* increased and a dark black color powder was formed. The UV radiation of sunlight reduced the oxidation state of iron in the presence of vitamin C present in *Triphala decoction* thereby

improving the bioavailability²⁶. The absorption of iron can be greatly influenced by vitamin C and tannin compounds. Ascorbic acid increased the bioavailability of iron by converting Fe^{3+} to Fe^{2+} , while tannin can reduce the bioavailability of iron. Hence, excess of ascorbic acid and/or a lack of dietary tannins have been suggested to overcome iron storage diseases²⁷. Due to the antagonistic properties of tannins present in *Triphala*, heavy absorption of iron is prevented. Punchihewa et al, (2022)²⁸ in their work, scientifically provided evidences on how a metallic iron gets converted to pure nanoparticles without impurity such as cadmium and chromium and also gets converted into human compatible

Fe^{2+} eliminating other undesired elements by *putapakha* process employed during purification.

Transformation of ferric to ferrous form by *Tamarindus indica* leaves

In traditional Iron – III oxide formulations, Fe_3O_4 (Ferric oxide) is the metal used and is of great therapeutic significance in the management of anemia. In all the traditional iron-based formulations, for purification of the iron, powdered Iron oxide – III was taken in a pot and mixed with four parts of *Tamarindus indica* leaves containing tartaric acid (Figure 3) and eight parts of water.

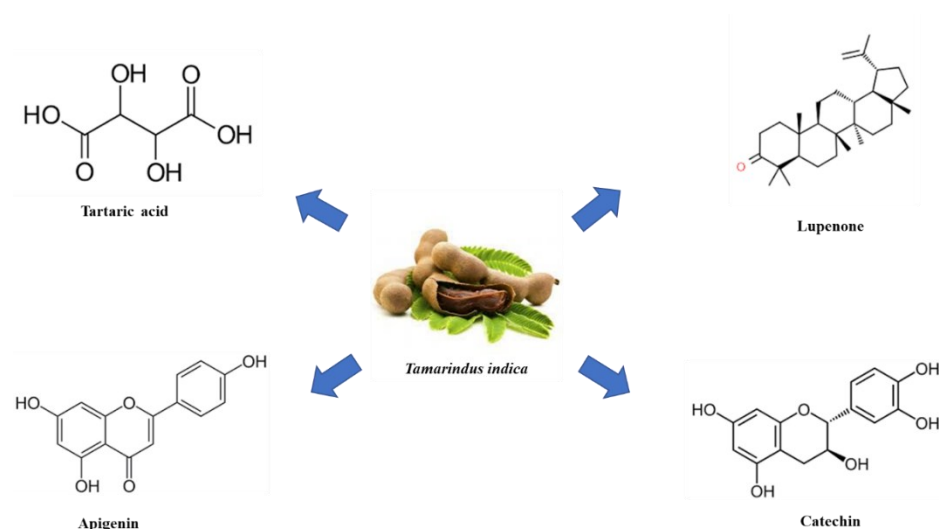


Figure 3. Major phytochemicals in *Tamarindus indica* decoction used in iron purification

This mixture was boiled for 3 h and then the powder was washed and dried in sunlight. X-ray diffraction study indicated the *madooram* preparation was completely transformed into $\alpha\text{-Fe}_2\text{O}_3$ form. The authors suggested that the herbal constituents²⁹⁻³¹ of *Tamarindus indica* may have transformed Fe_3O_4 into $\alpha\text{-Fe}_2\text{O}_3$ form³².

Wedelia calendulacea and *Citrus limon* in the formation of metal complex

Usage of *Wedelia calendulacea* (L.) Less plant juice containing luteolin, wedelolactone, kaurone and oridonin (Figure 4)³³⁻³⁵ is an alternative method for purification of Fe_3O_4 (Ferric oxide) based preparation (*Mandooram*). Fe_3O_4 (175 g) was soaked in Goat's

urine for 1 day and then equal quantity of *Wedelia calendulacea* juice and juice of *Citrus limon* were added and fried until the evaporation of the juices. Further, the FTIR spectra of the purified samples indicated the presence of functional groups including aromatic amines, sulfate ($\text{S}=\text{O}$), carboxylic acid hydroxyl ($\text{O}-\text{H}$), and alkane $\text{C}-\text{O}$ bonds, which indicated formation of herbo-metal complexes³⁶. Powders of iron and *madooram* were mixed with *Wedelia calendulacea* leaf juice in the preparation of traditional iron-based preparation *Aya bringaraja karpam*². In these iron-based preparations, *Wedelia calendulacea* contributed either in the formation of metal complex or enhancing the therapeutic efficacy, if administered in anemic conditions.

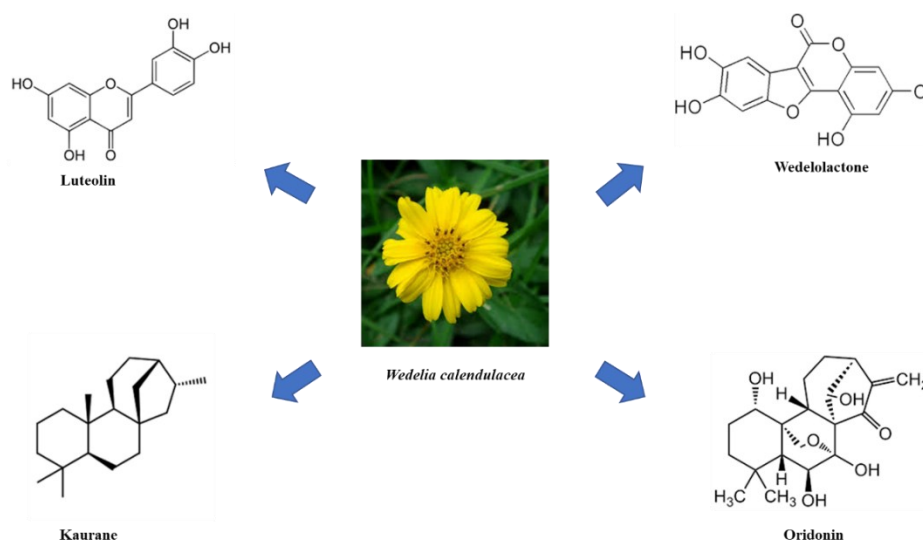


Figure 4. Major phytochemicals in *Wedelia calendulacea* leaves decoction used in iron purification

Juice of *Citrus limon* fruit was used in the preparation of various herbo-mineral formulations like *Mandooram*, *Annabethi chenduram*, etc. In *Annabethi chenduram*, iron was used in the form of ferrous sulphate ($\text{Fe}_2\text{SO}_4 \cdot 7\text{H}_2\text{O}$). In *Aya kantha chenduram* preparation, iron along with mercury sulphate, sodium chloride, rock salt, ammonium chloride was grounded with double the quantity of lemon juice (*Citrus limon*) containing narirutin, hesperidin, naringin and vicenin for two days, pelleted, dried and calcinated and administered for anemic condition². In an earlier study conducted by Rajalakshmi et al. (2017)³⁷, 500 ml of lemon juice (*Citrus medica*) was mixed with 500 g of purified iron and the mixture was kept under shaded condition for 12 h and dried under sunlight and then incinerated to prepare the *Annabethi chenthuram*. XRD analysis of *Annabethi chenthuram* indicated the increase of alpha (α) form of iron and removal of beta (β) form. In addition, FTIR spectra of the final product revealed the OH stretch (3200 cm^{-1})

and carbonyl groups (1623 cm^{-1}), that indicated the presence of functional groups of molecules present in *Citrus limon*³⁷.

Thus, the authors claimed that the herbal molecules of *Citrus limon* juice exhibited a significant role in the transformation of iron from its beta (β) to alpha (α) form. Besides, these plant molecules were also involved in the formation of herbo-metallic complex due to the presence of hydroxyl and carbonyl groups. Phytocomponents of lemon juice (**Figure 5**) identified through GC-MS indicated the presence of citric acid and other fragments suggesting the presence of amine groups, carboxylic groups and hydroxyl groups which can facilitate the formation of metal complex. Interaction of the terpenes of lemon juice with metals can enhance its therapeutic potential especially in the management of hepatic diseases like jaundice by acting as a hepatoprotective agent.

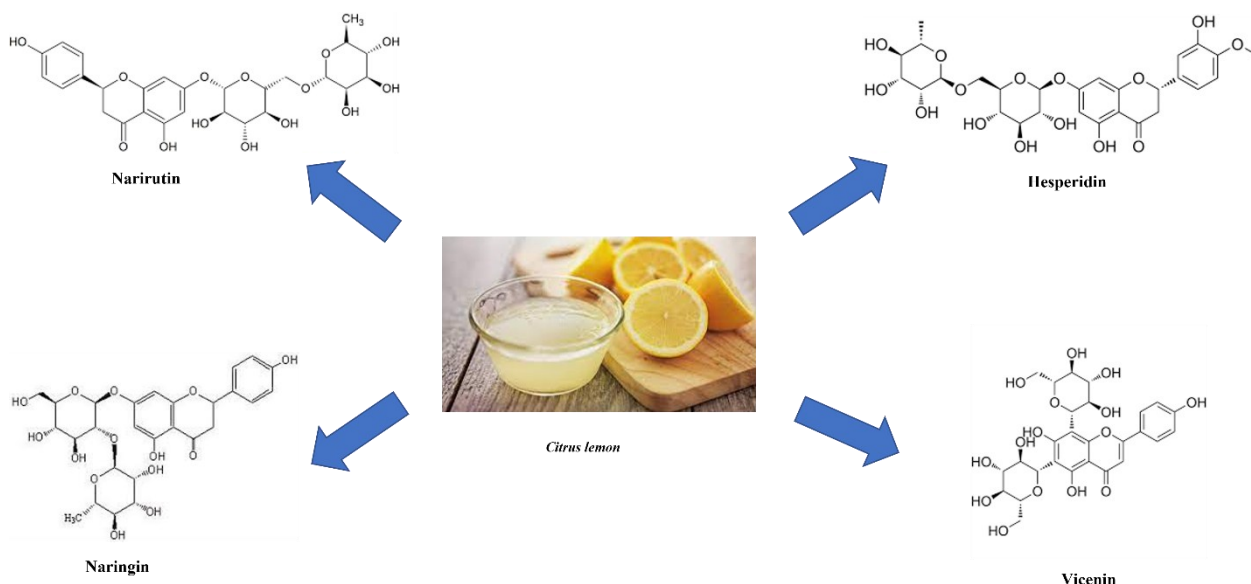


Figure 5. Major phytochemicals in lemon juice (*Citrus limon*) used in iron purification

***Aloe vera* in the complex formation and enhancement of therapeutic potential of Iron based formulations**

Iron was mixed with mercury, magnet, sulphur, rock salt and alum and grounded with *Aloe vera* juice containing phytochemicals like aloesin, aloenin, emodin and aloin-A (**Figure 6**)³⁸⁻⁴⁰, dried and calcinated in the preparation of *Arumuga chenduram* and used for treating all types of body pain

(Thiagarajan 2004). *Aloe vera* root juice is also used in the preparation of *Aya parpam* and *Aloe vera* leaf juice is used in the preparation of *Thiriloga chenthuram*⁸, and *Mandura chenduram*². Aloe as a calcinating agent enriched with quinones, contributed in the metal complex formation with OH and COOH groups present in the compounds and as an ingredient, enhanced the therapeutic potential against inflammation, joint pain and in controlling sugar levels.

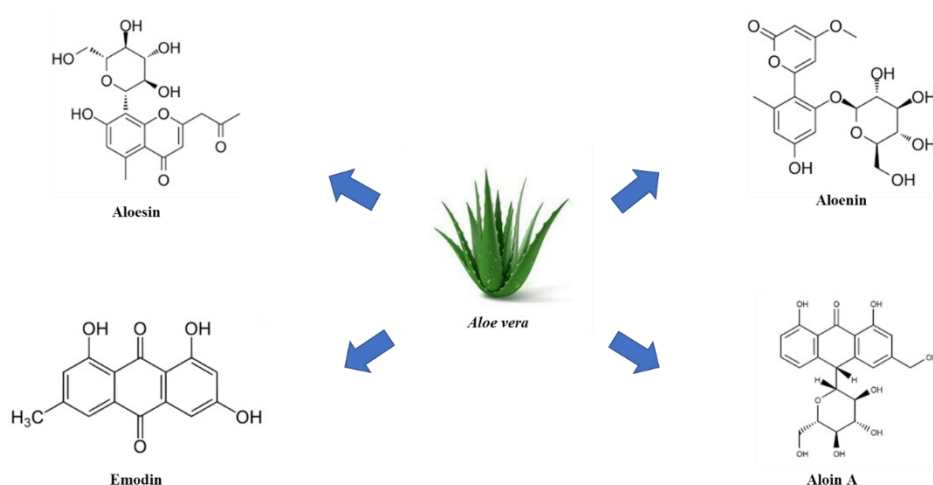


Figure 6. Major phytochemicals in Aloe vera leaves decoction used in iron purification

CONCLUSION

As various herbal ingredients are used to prepare iron-based traditional drugs, there are different dimensions regarding their role like purification of iron,

detoxification of iron, reduction of iron and formation of herbo-metallic complex. So, in the current review, scientific investigations conducted on the preparation of iron-based drugs using herbal ingredients were summarized to understand the actual role(s) of herbal

ingredients in the preparation of iron-based drugs. Based on the available research investigations, the possible role of herbal ingredients in the preparation of iron-based drugs could be: (i) Removal of inorganic impurities and incorporation of beneficial organic moieties into iron. (ii) Reducing iron from Fe^{2+} to Fe^{3+} form preventing the dangerous Fenton's reaction and thus toxicity of iron is removed and stabilized by iron-phytochemical complexes. (iii) Complexation of iron with herbal phytochemicals enhancing the thermal stability of iron during subsequent heating steps at high temperatures and also converting the gamma-form to biocompatible alpha-form of iron oxides.

Treatment with decoction of *Terminalia chebula*, *Terminalia bellirica* and *Phyllanthus emblica* fruits provided evidences on how a metallic iron gets converted to pure nanoparticles without impurity and also gets converted into human compatible Fe^{2+} by *putapakha* process employed during purification. Treatment process with various plant extracts/juices also enhance the therapeutic potential of a formulation. Although few studies have explained the formation of iron-phytochemical complexes and also illustrated the possible co-ordination structures, detailed analytical studies and therapeutic efficacy studies are necessary. Interaction of phytochemicals listed in this review from various herbals, which are used in the purification and preparation of iron-based traditional drugs need to be investigated for their possible complexation and stabilization functions.

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Conflict of Interest: The authors declare that they have no conflict of interest

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