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Research Article

EVALUATION OF CHELATING TENDENCY OF GALLIC ACID AS A DETOXIFYING AGENT: AN INNOVATIVE APPROACH

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ABSTRACT

During the last few decades, urbanization and industrialization has been increased enormously due to which chemicals have been used at a large scale. The industrial activities alter the natural flow of materials and introduce novel chemicals into the environment. Of the various sources of pollutants industrial effluents containing heavy metals pose a threat to the ecosystem. So, efforts have been made to minimize the toxification caused by heavy metals. The compounds like EDTA, DMSA, BAL etc. are being used for the chelation therapy since a very long time. Looking at the side effects caused by such compounds, the present research paper envisages the potential of gallic acid as a detoxifying agent. Gallic acid is a flavanoid which is extracted from peel of *Punica granatum*. The chelation of selected heavy metals (As, Hg, Cd and Pb) with gallic acid was carried out at 30°C at pH 5.8. Spectroscopic studies (Job's method and mole ratio method) were implemented to calculate the stability constants of synthesized complexes. The metal- ligand bonding was confirmed by FT-IR analysis of synthesized complexes. The present study reveals the potential of gallic acid as a bio chelator.

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INTRODUCTION

Nature has been a foundation of medicinal agents from ancient time and a remarkable number of modern drugs have been isolated from natural sources. In modern times inclination is observed towards traditional medicine and there has been an increasing demand for more and more drugs from plant sources. This resurgence of interest in plant derived drugs is mainly due to the current extensive belief that green medicine is safer and more dependable than the costly synthetic drugs many of which have unfavorable side effects. Some naturally occurring compounds like vitamin, amino acids have been found to be efficient during treatment of heavy metal toxicity [1]. Supplementation with a variety of vitamins and minerals has been suggested as a method to help augment the elimination of toxic metals, either by chelation or the effects of antioxidants [2]. Some agents, such as algal polysaccharides and chlorella are thought to bind certain metals enhancing elimination. Cilantro has been reported to enhance mercury elimination via unknown mechanisms, although evidence remains limited [3]. Glutathione is recurrently recommended as a physiologic chelator and antioxidant [4]. N-acetylcysteine

(NAC) is a sulfhydryl group donor and acts as a precursor for glutathione in the liver. It also has anti-oxidant and free radical scavenging properties. Although, it has been scientifically proven as an efficient antidote for acetaminophen toxicity [5], its role in chelation or treatment of heavy metal toxicity is uncertain [6]. Other anticipated supplements for metal toxicity take account of methionine, taurine, alpha lipoic acid, ascorbic acid, and selenium among others [7]. Taurine and methionine are sulphur containing amino acids which decrease oxidative stress markers resulting from heavy metal exposure [8,9]. Adverse effects of these agents, when taken in moderate doses are generally low; however, their efficacy in treating heavy metal toxicity has not been scientifically proven.

Naturally, some plants are considered as important source of nutrition and their use is recommended for their therapeutic values. Plants can make available biologically active molecules and endow with structures for the development of modified derivatives with enhanced activity and reduced toxicity.

Chelation therapy involves conventional chelating agents to detoxify heavy metals but despite obvious advantages, these agents have certain undesired features [10]. The naturally

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occurring compounds which can be used as potential chelating agents are called biochelators. In present work, biologically active molecule, gallic acid was selected as ligand for complexation with selected heavy metals (As, Hg, Cd and Pb). The complexation of arsenic, mercury, cadmium and lead was carried out with gallic acid. Further, stoichiometric ratio and stability constants of coordination complexes were also calculated which were found to be quite effective. Gallic acid was extracted from peel of *Punica granatum*.



Fig 1 Plant of *Punica granatum*

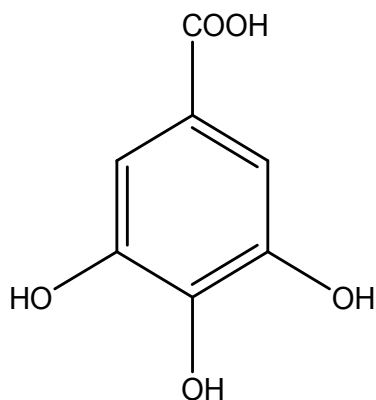


Fig 2 Molecular structure of gallic acid

MATERIALS AND METHOD

Equipments used

The spectrophotometric measurements were carried out on a UV – 1700 Shimadzu double beam spectrophotometer (Japan) using matched 10 mm quartz cells. The spectra of compounds under investigation in infra red absorption region were obtained on FT- IR PerkinElmer spectrum version 10.4.00 in KBr disc.

Collection of plant materials

Pomegranates (*Punica granatum*) were obtained from local markets. The peel was manually removed, shade-dried and powdered.

Extraction of gallic acid from pomegranate peel

Powder was extracted with a Soxhlet extractor using methanol for 4 hours [11]. The extract was filtered through Whatman No.41 filter paper for removal of peels particles and concentrated under vacuum at 40°C. The dried extract powder was further re-dissolved in methanol.

Spectrophotometric determination of complexes

Continuous variation method

1. Preparation of stock solutions of heavy metal ions:
2. Stock solutions of 1.00×10^{-2} M heavy metal ions were prepared by dissolving requisite amounts of arsenic chloride, mercuric chloride, lead chloride and cadmium chloride in water separately.
3. Preparation of stock solution of biochelator: $\times 10^{-2}$ M stock solution of gallic acid was prepared by dissolving requisite amount of gallic acid in water.
4. The absorption spectra were recorded over the wavelength range of 200 to 800 nm. The values of λ_{max} were determined for all the four coordination complexes which came out to be 290 nm, 340 nm, 290 nm and 320 nm for lead – gallic acid, cadmium – gallic acid, mercury – gallic acid and arsenic – gallic acid complexes respectively and these values were used for analytical measurements.
5. Spectrophotometric determination by Job's method was carried out as per procedure discussed above. A series of solutions were prepared by mixing 1 to 9 ml of stock solution of arsenic chloride, lead chloride, cadmium chloride and mercury chloride with an aliquot of gallic acid in such a way that the mole fraction of the solution remained constant. The wavelength of maximum absorbance was noted against the reagent blank for each of the metal complex. All the measurements were made at their respective wavelength for the concerned complex at 30°C.

Mole ratio method

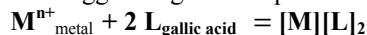
To a series of solutions containing 2 ml of each metal ion (arsenic chloride, lead chloride, cadmium chloride and mercury chloride) and increasing amounts of gallic acid volumes were added. Each solution was treated as per the method discussed above. All the measurements were made at wavelength of maximum absorbance for each metal complex.

Gallic acid-heavy metal complexes

The stability constants of metal (As, Cd, Pb and Hg) - gallic acid complexes were determined by Job's method of equimolar solutions with the help of the formula given as follows:

The stoichiometric ratio of metal to gallic acid was determined by mole ratio method. The curves for all the four metals – gallic acid complexes displayed maximum absorbance at mole fraction $X_{\text{metal}} = 0.3$, which indicates the formation of complex with metal ion to ligand ratio 1:2.

The suggested general equation for the complexes is:



The graphical representation of data for complexation reactions of selected heavy metals with gallic acid observed by Job's method and mole ratio method is depicted in fig. 3 to 10.

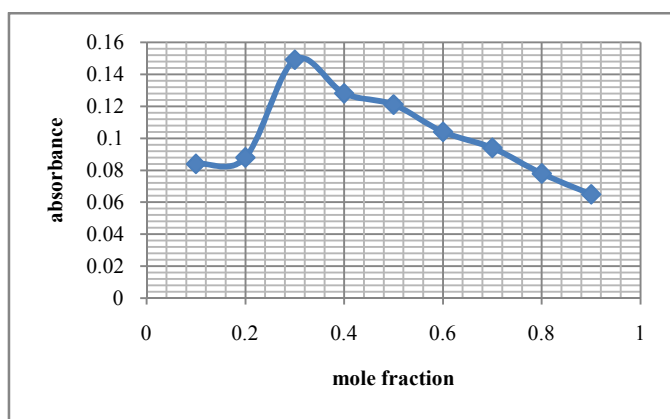


Fig 3 Pb- Gallic acid curve by Job's method

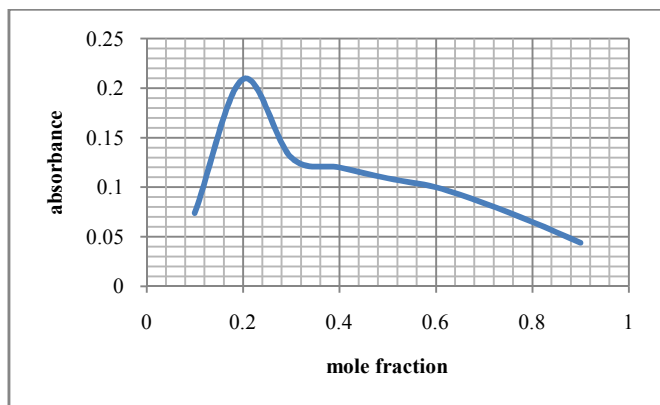


Fig4 Cd-gallic acid curve by Job's method

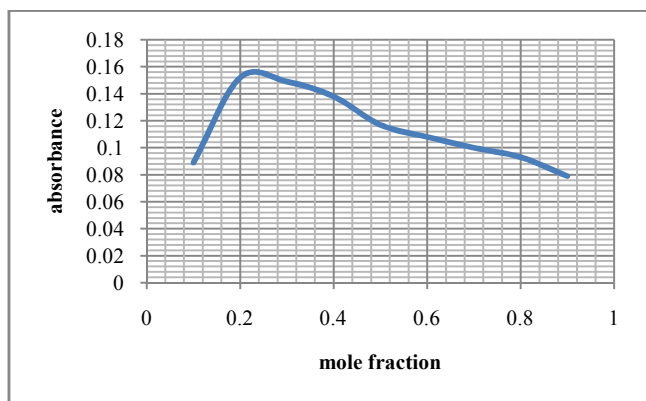


Fig 5 Hg- gallic acid curve by Job's method

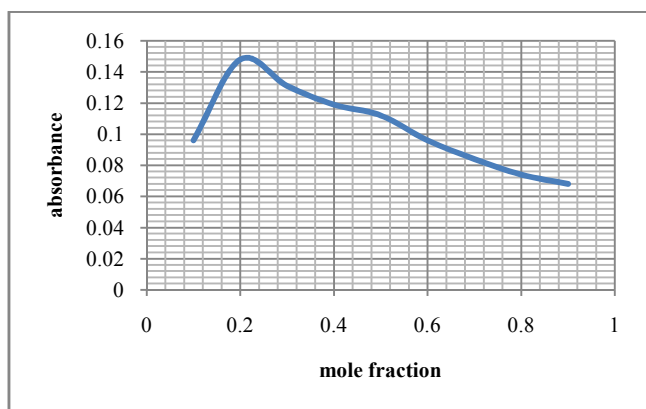


Fig 6 As - gallic acid curve by Job's method

By using the mole ratio method, at constant metal concentration (for As, Hg, Pb and Cd each) and varying gallic acid concentrations at their absorption maximum, a sharp band was observed at 1:2 mole ratio of metal and ligand.

The corresponding equation for the mole ratio method is as follows:

$$K_{st} = \frac{A/\epsilon b}{[C_{\text{metal}} - A/\epsilon b] \times [C_{\text{gallic acid}} - A/\epsilon b]}$$

Where ϵ = molar absorptivity constant, A = absorbance at peak point.

ϵ is dependent upon wavelength and is called molar absorption coefficient and has units of $L \text{ mol}^{-1} \text{ cm}^{-1}$. The use of this symbol specifically requires that the concentration is expressed in units of molarity and sample path length in cm.

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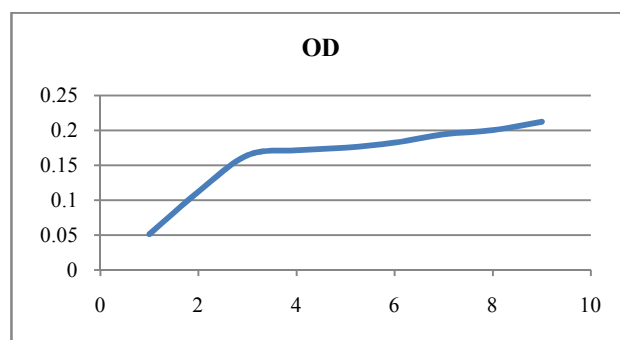


Fig 7 Hg- gallic acid curve by mole ratio method

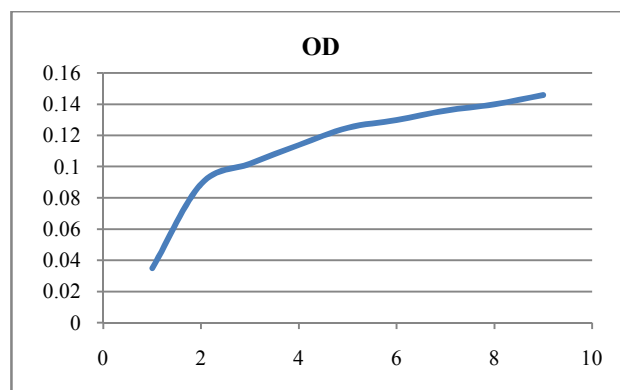


Fig 8 As-gallic acid curve by mole ratio method

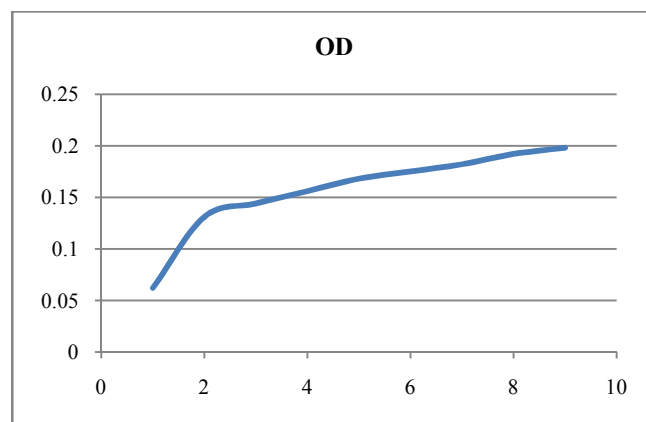


Fig 9 Pb- gallic acid curve by mole ratio method

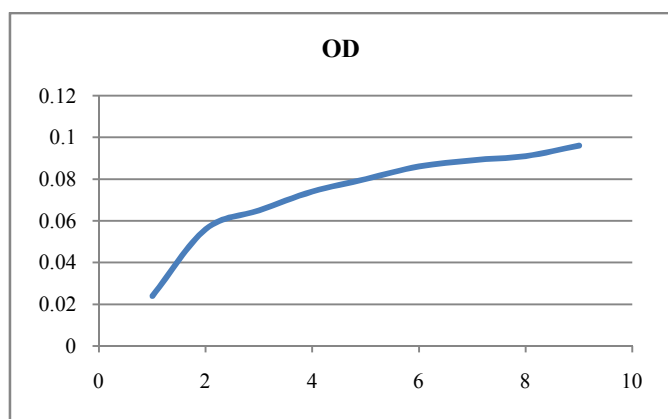


Fig 10 Cd-gallic acid curve by mole ratio method

Stability constants of coordination complexes were calculated by using above data and graphs, which are revealed in the table 1:

Table 1 Stability constants of metal – gallic acid complexes

S.No.	Name of the complex	Metal: Ligand	Stability constant
1.	Arsenic-gallic acid complex	1:2	4.8×10^7
2.	Cadmium-gallic acid complex	1:2	7.3×10^6
3.	Mercury- gallic acid complex	1:2	6.9×10^6
4.	Lead-gallic acid complex	1:2	2.72×10^8

FT-IR analysis

Gallic acid vibration

In the region of hydrogen bonded OH groups ($3500-3200\text{ cm}^{-1}$) a strong wide band at around 3400 cm^{-1} was observed in the gallic acid spectrum. The band was assigned to the stretching vibrations of hydrogen bonded phenolic hydroxyl groups ($\nu(\text{OH})$) [12]. The corresponding bands were observed in gallic acid-Cd, gallic acid-Pb, gallic acid-Hg and gallic acid-As spectra. The bands due to C=O stretching vibrations that appeared at 1715 cm^{-1} indicated the presence of aromatic carbonic acids.

Metal – gallic acid vibration

The complex formation of heavy metals with gallic acid was characterized by IR spectroscopy. For IR study the complex was obtained at molar ratio of selected heavy metals (As, Hg, Cd and Pb) and ligand (gallic acid) equal to 1:2. From the IR spectra of gallic acid and synthesized heavy metal complexes of gallic acid, it is clear that there is slight shifting in $-\text{OH}$ absorption towards lower range which indicates involvement of $-\text{OH}$ group in coordination bonding with metals. It has been reported in earlier studies as well that $-\text{OH}$ groups in gallic acid are responsible for chelating tendency of gallic acid [13]. The absorption band in metal complexes around the region 600 to 400 cm^{-1} may be attributed to metal – ligand bonding [14]. This band is not observed in IR spectrum of gallic acid. The changes in the spectra profile in the region $1300-1000\text{ cm}^{-1}$ prove that phenolic oxygen is involved in the coordination of metal ion. The proposed structure of heavy metal complex of gallic acid in fig 11 agrees well with the obtained IR spectra. The IR data suggest that probably phenolic oxygen are involved in the coordination of metal ions (As, Hg, Pb and Cd) with gallic acid.

Table 2 Comparison of infra red spectral data of gallic acid and gallic acid-metal complexes

S.No.	Compound	ν_{OH}^{-1} cm	$\nu_{\text{C=O}}^{-1}$ cm	$\nu_{\text{C=C}}^{-1}$ cm	$\nu_{\text{C-OH}}^{-1}$ cm	$\delta_{\text{C-OH}}^{-1}$ cm	γ_{OH}^{-1} cm	M-O ⁻¹ cm
1.	Gallic acid	3414 3377	1716	1616 1512	1454	1226		
2.	Cd-gallic acid	3414 2925	1724	1619	1118		812	618
3.	As-gallic acid	3400 2937	1719	1619	1182	1060	777	631
4.	Hg-gallic acid	3434 2924	1735	1613	1347	1052	877	441
5.	Pb-gallic acid	3401 2925	1554	1410	1337	1051		617

The proposed structure of heavy metal complex with gallic acid as biochelator is given as:

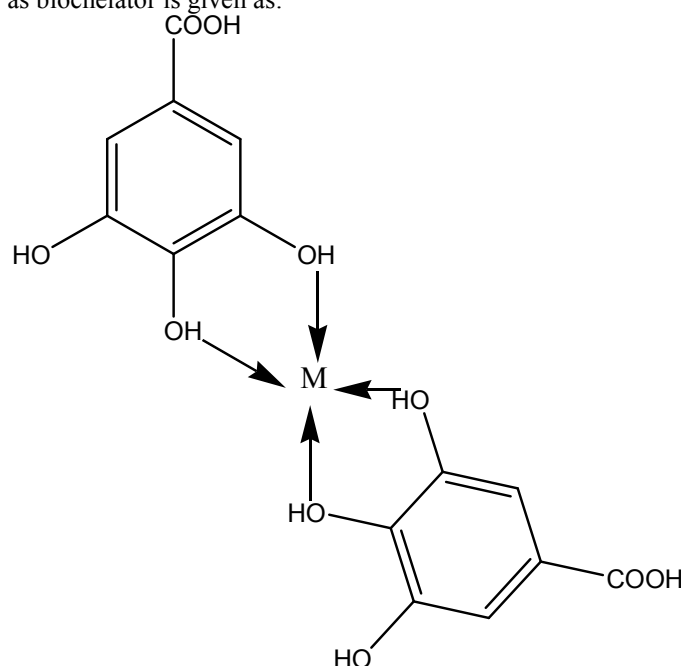


Fig. 11 Proposed structure of heavy metal complex with gallic acid

CONCLUSION

The article presents the therapeutic potential of gallic acid as a detoxifying agent. Complexes of As, Cd, Hg and Pb with gallic acid are found to have metal to ligand ratio as 1:2 (ML₂), where M is metal and L is gallic acid. The present study envisages the chelating tendency of gallic acid, extracted from pomegranate which is widely available to people. The significance of this study is use of gallic acid as a bio chelator as compared to synthetic chelators which have severe side effects. The most important problem concerning the medical use of synthetic chelating agents is their low therapeutic range, which is mainly due to the inherent toxicity of the chelator itself. Gallic acid, being a bio chelator, has the possible beneficial effects of removal of toxic metals in people with low-level exposure without overt symptoms of toxicity. So, being a bio chelator and due to its easy availability, gallic acid can be used in heavy metal detoxification effectively.

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