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RESEARCH ARTICLE

Modeling and Optimization of Extraction of Gallic Acid from Chenopodium Murale using Response Surface Methodology

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Abstract

In this work, the investigation of recovery of gallic acid from chenopodium mural by leaching process was conducted. 99% of ethanol was used as a solvent. Five parameters were investigated namely time (20 - 90) min, speed of mixing (200-1000) rpm, temperature (25˚C-70˚C), particle size (100-500) µm, solid/liquid ratio 1/50 gm/gm to 1/20 gm/gm. To design the experiments, Response Surface Methodology was used using Minitab 17 software. The model equation for optimization of the extraction process was found. The best conditions for the process were extraction temperature of 70 ˚C, the liquid-solid ratio of 0.05 gm/ml, extraction time of 90 min, agitation speed of 200 rpm and particle size of 100 microns. HPLC instrument equipped with UV detector UV-20A with wavelength Range 190-700nm was used for the analysis of samples. The aim of this study is to obtain a model equation for optimization of extraction of gallic acid from Chenopodium murale using response surface methodology. The influence of temperature, solid/liquid ratio, agitation speed, particle size and time on extraction yields will analyze.

Keywords: *Antioxidant, Gallic acid, Chenopodium mural, Leaching and Response Surface Methodology.*

Introduction

The antioxidant can be defined as any molecules able for preventing or delaying oxidation by loss one or more electrons from other molecules [1].Cancer has been widespread disease in the world. Colorectal cancer is noticed as the third the most a widespread cancer type, using of controlled drug as capsules to treat cancer disease is become more popular in the world, oxidation reactions are important for life but also they can be damaged, the first operation in the production of drug is the extraction of raw material from the herbal plant.

Plants and animals contain a complex system of multiple types of antioxidants as glutathione, vitamin C, vitamin A, and vitamin E also contain enzymes as catalase, superoxide dismutase and various peroxides, good main source of antioxidant are herbal medicines and dietary foods , these are protected peoples from the damage caused by free radicals [2]. Gallic acid (3, 4, 5-trihydroxybenzoic acid) is a natural polyphenolic compound found in processed drinks such as tea. It can be found in the plants in the form of free acids, esters, catechin derivatives and hydrolysable tannins [3].

The method of extraction is a very important step for the use of phenolic compounds. The type and the quantity of the phenolic compounds obtained from herbs are very affected by the extraction method. Soxhlet extraction which is found in nineteenth century which is developed by F.Soxhlet which is summed up by taken a suitable quantity of herbs contain gallic acid in a suitable quantity of good solvent such as ethanol. These methods of extraction take more than 7 hours and then filtered under vacuum using a rotary evaporator.

These methods consume a lot of time and use a complex stomach. A different types of extraction techniques have been developed include Ultrasonic assisted extraction (UAE). This method was performed by adding a quantity of herbs sample in a good solvent and the flask immersed in ultrasonic bath. The disadvantage of this method is known for its low efficiency and potential environmental hazards due to the high demand for organic

solvents. Another method of extraction which is microwave assisted extraction (MAE) it was carried out using domestic microwave. B both UAE and MAE methods require a small amount of solvent and the time require less than soxhlet extraction method but the local temperature increase quickly which cause cavity effect so the optimization of extraction conditions is necessary [4].

E.M silva et.al (2007) applied response surface methodology of a set of 18 experiments to show the effect of temperature, time and the ethanol proportion to extract phenolic compounds from *Inga edulis* leaves, the optimized concentration of gallic acid was 134.6 mg gallic acid equiv./g dry matter. The conditions were temperature 58.2˚C, time of contact 46.8 min and ethanol proportion 86.8% [5].

Stefania mylonaki et.al (2008) investigated the optimizing recovery of phenols from olive leaves by using reusable and nontoxic solution, the extraction is a media composition from water, ethanol, and citric acid. The factors considered were ph of the medium, the time of extraction and ethanol proportional.

The maximum theoretical yield was 250.2± 76.8 mg gallic acid equivalent per gm of dry chlorophyll-free tissue were conditions are ethanol proportional 60%, ph 2 and time of 5 hours [6].Entessar h.a.al-mosawe et.al (2012) this studied the extract of gallic acid from rind of pomegranate by using soxhlet extraction, the solvent is ethanol/water (40/60) and then identified in chromatography method using FTIR, UV and HPLC) [7].

Mohammad Hossain et.al(2012) optimized the ultrasound assisted extraction (UAE) conditions to maximize the antioxidant activity of total phenol content of individual polyphenols of the extracts from four Lamiaceae herbs namely marjoram, oregano, rosemary and sage under conditions ranging regard to amplitude of sonication (24.4-61) μm, extraction temperature of (15-35)ºC and the time (5-15) min were identified using response surface methodology [8].

Giri Raj Gnawali et.al (2013) isolated Gallic acid from ethyl acetate soluble portion of the methanol extract of fruit pulp of Terminalia chebula and characterized by comparing the melting point, Rf values, UV and IR spectra with authentic gallic acid. Quantitative determination of phenolic from different extracts of medicinal herbs such as Adhatoda vasica Nees, Bergenia ciliata Sternb, Phyllanthus emblica Linnaeus, Terminalia bellirica (Gaerth) Roxb, Terminalia chebula Retzius and Vitex negundo Linnaeus which are commonly used as home herbal remedies for the primary health care was carried out using Folin-Ciocalteu colorimetric method.

The highest amount of gallic acid was detected 70% acetone extra of B.ciliata (357.8mg GAE/g sample) and the lowest amount was detected in 50% aqueous methanol extract of T. bellirica (108.69mg GAE/g sample)[9]. Isabel Rodríguez Amado et.al (2014) made a study reports to optimize the conditions (temperature, ethanol and processing time) for antioxidant extraction from potato peel (Agria variety) waste.

At short extraction times (34 min), optimal yields of phenolic (TP) and flavonoid (FV) compounds were reached at 89.9ºC and ethanol concentrations of 71.2% and 38.6% respectively[10]. Luping Kang et.al (2015) stated that the Penthorum chinense Pursh is rich in gallic acid, which has not only antioxidant also contain anti-inflammatory, antifungal and antiunor activities.

To optimize their extraction conditions, various extraction parameters were chosen to identify their effects on gallic acid extraction. [11].Siti Kusmardiyani et. al. determine antioxidant activity from various herbs extracts of three kinds of Lemongrass using two antioxidant testing methods which are 2,2-diphenyl-1-picrylhydrazyl (DPPH) and ferric reducing antioxidant power (FRAP) and correlation of total phenolic content (TPC), and total carotenoid contents (TCC) with their inhibitory concentration 50% (IC50) of DPPH and exhibitory concentration 50% (EC50) of FRAP [12].

Ali Abdulkadhm Jasim Al-Ghanimi (2016) studied some parameters for optimizing conditions of gallic acid extraction from Eucaldulensis leaves. Results show the maximum yield of gallic acid (GA) was obtained by using ethanol 50% as extraction solvent at 40ºC for 24 hours [13].

Xin-Hong Wang et.al (2016) investigated the extraction of gallic acid from Suaeda glauca Bge using Ultrasound assisted extraction (UAE). The conditions were ethanol 70% as

extraction solvent, temperature, solid/liquid ratio and extraction time. The results show that the maximum levels of gallic acid is 6.3mg/gm at 51ºC, 19.52 ml/gm and 42.68 min [14]. Burcu OZTURK et.al (2017) optimized the microwave extraction of total flavonoids from Nigella sativa with methanol by using response surface methodology based on Box-Behnken design. Microwave extraction experiments have been carried out with the parameters of microwave power, solid/liquid ratio and the extraction time[4].

Materials and Method

Material

Chenopodium murale was obtained from the garden of the Department of Pharmacognosy College of Pharmacy. The identified is made in the College of Sciences University of Baghdad. The leaves were cleaned, shade dried and powdered in an electric grinder.

Solvent

Ethanol 99.9% concentration which supplied by United Arab Emirates by Asia Petrochem. This type of ethanol is used in pharmaceutical industries. Ethanol is a select a solvent of low viscosity in order to accelerate mass transfer.

A apparatus

The material was grinded by The electric grinder (Gosonic), sieved to the desired particle size of 100 microns, 300 microns and 500 microns by sieve analysis (Endecotts). The magnetic stirrer supplied by ISO LAB Company (Germany) was used for this experimental work. The maximum stirring capacity is 3 liters. The speed range is from 100 to 1500 rpm. The speed and temperature display are LED. The heating input is 500 watt. The heating range is room temperature to 280ºC. The apparatus is under temperature and rpm controllers. Figure 1 shows the photo of the apparatus.

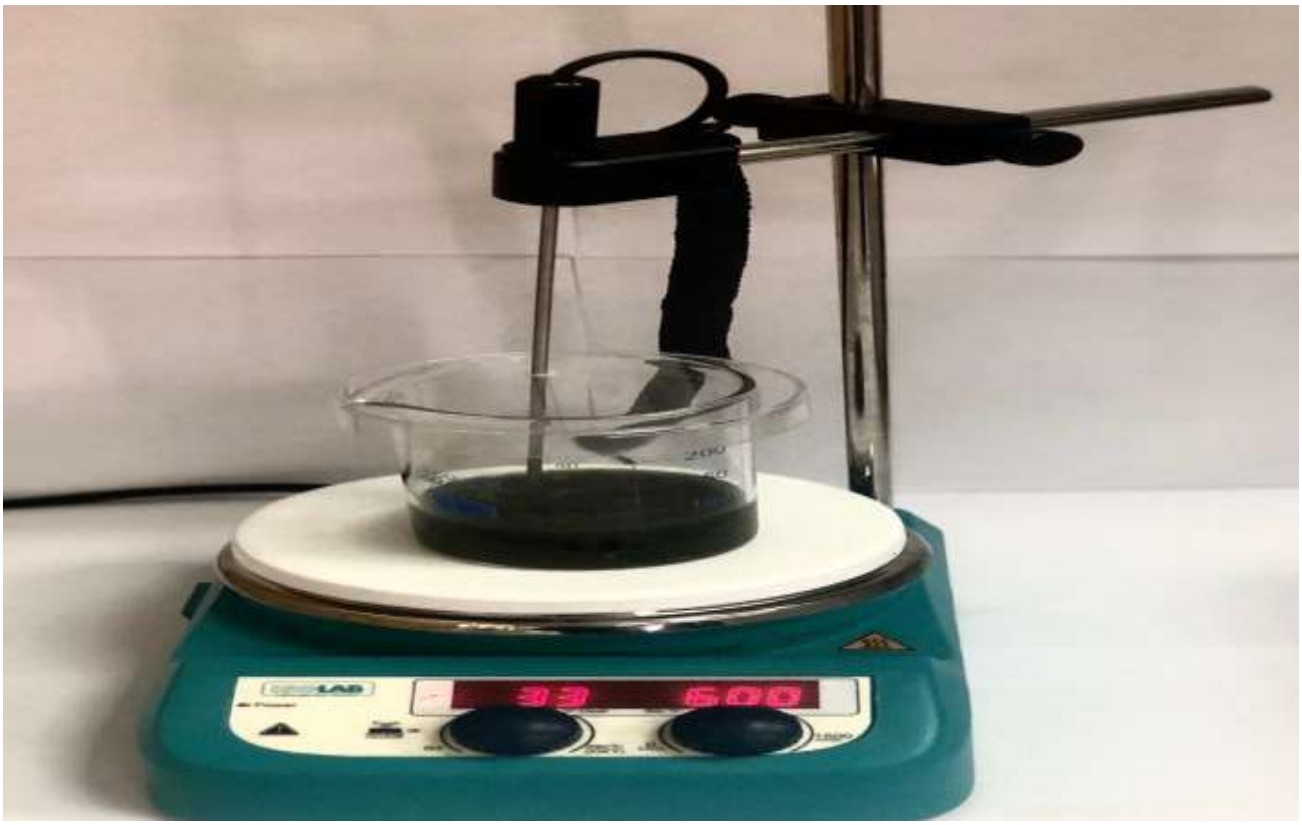

Figure 1: The photo of the experimental apparatus

Method

Five parameters were investigated namely time, sped of mixing, temperature, particle size, solid/liquid ratio. The variables were varied as follow: - temperature (25˚C - 70˚C), time (20 - 90) min., mixing (200 - 1000) rpm, Particle size (100 - 500) µm and the solid/liquid ration was taken from 1/50 gm/gm to 1/20 gm/gm. To design the experiments, Response Surface Methodology was used using Minitab 17. The conditions are specified in table 2. 100ml of 99.9% ethanol as a solvent was used for all the experiments. At the end of the specified extraction conditions of each experiment, the

content of the flask was filtered through 110 mm filters (Whatman filter paper). Samples were analysis to find the amount of gallic acid by high performance liquid chromatograph. The chromatography was performed on a Shimadzu LC- 10AT; HPLC instrument equipped with UV detector UV-20A with wavelength Range 190-700nm. C18 (2) (4.6 x 250mm, 5µ particle size).Table 1 shows the result of the experimental design. Table 1 shows the results of experimental design using Minitab software.

Table 1: the results of experimental design using Minitab software

s.	Time(min) = X_1	Temperature (C°)= X_2	Agitation speed (rpm)= X_3	Particle size (micron) = X_4	Solid/liquid ratio (gm/gm) =X_5	Concentration (µg/ml)
1	55	48	600	500	0.035	7.8655
2	20	70	1000	100	0.05	15.6127
3	55	48	600	100	0.035	11.5415
4	90	25	1000	100	0.05	9.1182
5	55	48	600	300	0.035	4.9518
6	90	25	200	500	0.05	4.9196
7	20	70	1000	500	0.02	5.6694
8	90	48	600	300	0.035	6.9453
9	55	48	600	300	0.035	4.9548
10	90	25	200	100	0.02	3.1700
11	20	48	600	300	0.035	4.1235
12	20	25	1000	100	0.02	3.9544
13	90	70	200	100	0.05	33.1254
14	55	70	600	300	0.035	12.5493
15	20	25	200	500	0.02	1.3914
16	55	48	600	300	0.02	1.0235
17	90	70	1000	100	0.02	18.4701
18	55	48	600	300	0.05	6.5952
19	55	48	600	300	0.035	4.8596
20	55	48	600	300	0.035	4.8796
21	55	48	600	300	0.035	4.9113
22	90	25	1000	500	0.02	1.9854
23	90	70	200	500	0.02	8.7022
24	20	25	200	100	0.05	6.8357
25	20	25	1000	500	0.05	1.9156
26	20	70	200	100	0.02	11.0624
27	55	25	600	300	0.035	1.0254
28	55	48	1000	300	0.035	2.7426
29	55	48	200	300	0.035	5.0234
30	90	70	1000	500	0.05	17.8035
31	20	70	200	500	0.05	24.5916
32	55	48	600	300	0.035	4.9681

Results and Discussion

Modeling

The results in Table 1 was used to constricted the equation described the model of the recovery of gallic acid

Let time is X_1, temperature is X_2, agitation of speed is X_3, particle size is X_4, solid/liquid ratio is X_5

$Y= 1.18 – 0.0701\ X_1 – 0.292\ X_2 + 0.01973\ X_3 – 0.06527\ X_4 + 379\ X_5 +$

$0.000589\ X_1*X_1 + 0.00418\ X_2*X_2 – 0.000006\ X_3*X_3 + 0.000122\ X_4 *X_4 – 4458\ X_5*X_5 + 0.001275\ X_1*X_2 + 0.000063\ X_1*X_3 – 0.000237$

$X_1*X_4 + 0.686\ X_1*X_5 – 0.000143\ X_2*X_3 – 0.00012\ X_2*X_4 +6.463\ X_2 *X_5 – 0.000004\ X_3*X_4 – 0.3206\ X_3*X_5$ 1

Effect of Temperature

The effect of temperature on gallic acid recovery was shown in Figure 4 under the conditions of 90 min, the particle size of 100 µm, agitation speed of 200 min^{-1} and the solid/liquid ratio of 0.05 gm/gm. It's clear from the Figure that the concentration of gallic acid is increasing with temperature

increasing. The values of concentration are 11, 14.8, 19.55, 25 and 31 µg/ml when using temperature of 30, 40, 50, and 60 ºC respectively after 80 min. Increasing the temperature cause decreasing in viscosity and this leads to improves the mass transfer process due to the increase in diffusion rate, high solubility also increases in collision frequency of molecules [15].

Also according to the Arrhenius equation, the temperature will affect the dissolution rate as shown in equation 2:

$$K = K_{\circ} e^{\frac{-E}{RT}} \quad \text{.....2}$$

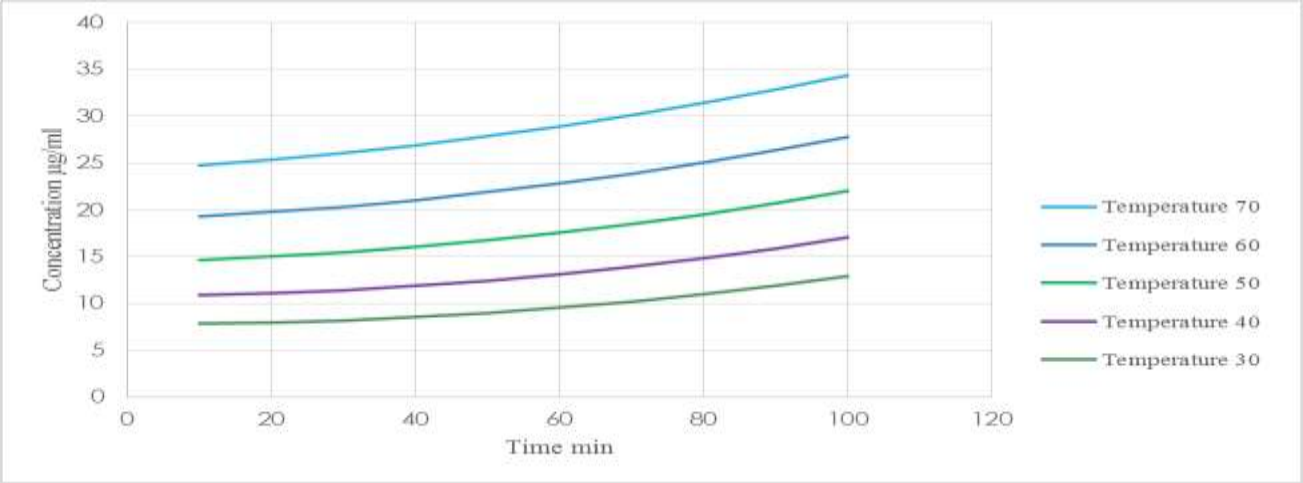

Figure 4: The effect of temperature on the gallic acid concentration at conditions: 200 min^{-1}, 100µm, 0.05gm/gm and 90min

Effect of Solid/liquid Ratio

The effect of the solid/liquid ratio is shown in Figure 5 under conditions of a temperature of 70ºC, time of 90 min, agitation speed of 200 min^{-1}and particle size of 100µm. The concentration are 9, 16, 22, 27 and 31.5 gm/l for 0.01, 0.02, 0.03 0.04 and 0.05 solid/liquid ration respectively after 80 min. It's clear from these results the ability of the solvent to dissolve the solid and there is no saturation in the solubility of solid. Decreasing the solid liquid ratio mean sufficient solvent available and hence improving the driving force of the leaching process. It's an n important factor in influencing the extraction of gallic acid, its concerns the contact area between raw material and solvent (13).The decrease of extraction of gallic acid with the increase of solvent quantity.

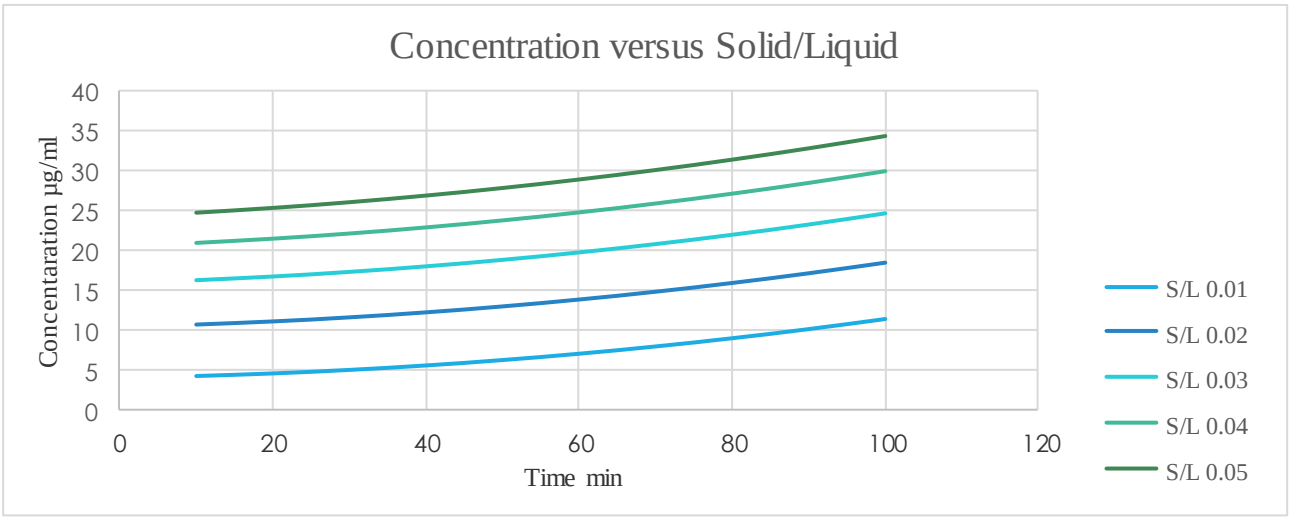

Figure 5: The effect of solid/liquid on the gallic acid concentration at conditions: 70ºC, 100µm, 90min and 200min^{-1}

Effect of Agitation Speed

The effect of agitation speed is shown in Figure 6 under the conditions of temperature of 70ºC, particle size of 100 µm, time of 90 min and solid/liquid ratio of 0.05 gm/gm., the results showed at 90 min when the speed is 1000 min^{-1}the concentration is 26.2679,

28.6359, 30.5239, 31.9319 and 32.8599 µg/ml for 1000, 800, 600, 200 and 200 min^{-1} respectively. In general, the agitation influence reduces the liquid film thickness formed around the particles, the diffusion through the boundary layer of the leach reagent toward the external surface of the particle eases[16]. In this experimental work there is an adverse effect of the agitation speed when increasing of speed the concentration of gallic acid decrease, this may be attributed to the collision of small partials to for larger one and when the number of particles per unit area will increase the resistance to fluid will increase and hence the recovery will decrease.

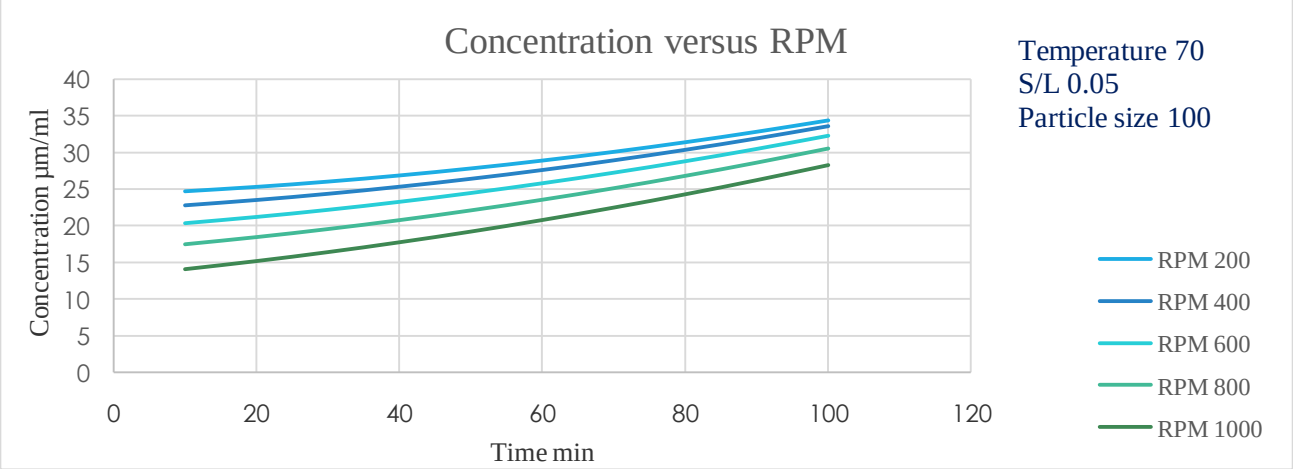

Figure 6: The effect of agitation speed min^{-1} on the extraction of gallic acid at conditions: 70°C, 90 min, 0.05 gm/gm, 100 µm

Effect of Particle Size

Figure 7 shows The effect of particle size on the recovery of gallic acid while the other variables are constant(temperature of 70°C, solid/liquid ratio of 0.05 gm/gm and agitation speed of 200 min^{-1}), the results show that the concentration after 90 minutes are 24.2, 27.3 and 32. 9 µg/ml for the particles size of 300, 200 and 100 µm respectively. The smaller particle size is the larger surface area available for contact between the liquid and solid. The distance that must the liquid passing throw the solid will decrease with decreasing the particle size so the resistance to diffusion will decrease, hence the mass transfer process improves and the recovery of gallic acid increase.

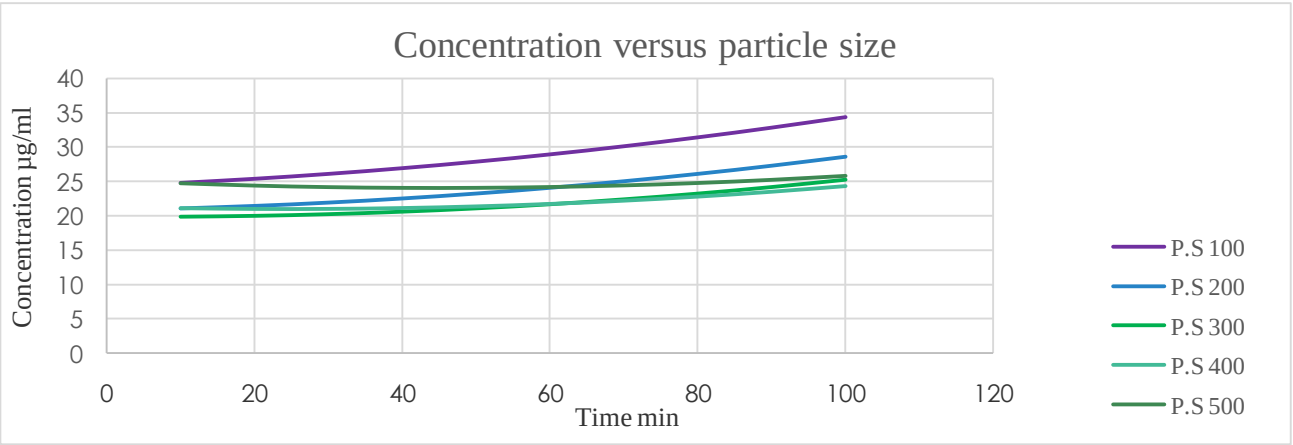

Figure 7 the effect of particle size on the concentration of gallic acid at conditions: 70°C, 90 min, 200 min^{-1}, 0.05 gm/gm

Conclusion

In this work, an efficient method has been established for the extraction of gallic acid from *Chenopodium murale*. The extraction process was optimized by response surface method in order to obtain satisfactory extraction efficiency .The results proved that the ethanol was a good solvent for the extraction of gallic acid and possessed the highest extraction efficiency in selected ionic liquid under the extraction conditions: extraction temperature of 70 ˚C, liquid-solid ratio of 0.05 gm/ml, extraction time of 90 min, agitation speed of 200 rpm and particle size of 100 micron ethanol absolute solution using Leaching technique.

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