Journal of Neonatal Surgery
ISSN(Online): 2226-0439
Vol. 14, Issue 32s (2025)
https://www.jneonatalsurg.com

OPEN ACCESS

Development and Evaluation of Gallic Acid- Loaded Solid Lipid Nano-particles

Arpit Singh[1], Manoj Bhardwaj[*2]

[1]Research Scholar, Devsthali Vidyapeeth College of Pharmacy, Lalpur, Rudrapur, Uttarakhand

[*2]Professor, Devsthali Vidyapeeth College of Pharmacy, Lalpur, Rudrapur, Uttarakhand

***Corresponding author:**

Prof. (Dr.) Manoj Bhardwaj

Professor, Devsthali Vidyapeeth College of Pharmacy, Lalpur, Rudrapur, Uttarakhand

Cite this paper as: Arpit Singh, Manoj Bhardwaj, (2025) Development and Evaluation of Gallic Acid- Loaded Solid Lipid Nano-particles. *Journal of Neonatal Surgery*, 14 (32s), 7242-7255.

ABSTRACT

The current study was based on the Development and Evaluation of Gallic Acid- Loaded Solid Lipid Nano-particles. Gallic acid was purchased from the Oxford Lab Fine Chem LLP, India. Stearic acid, Span 20, Tweens 80 (Sigma Aldrich, India), distilled water, ethanol were procured from the local chemical shop in Haridwar, UK. In Preformulation studies, various parameters i.e., organoleptic properties, melting point, solubility, Drug excipients compatibility studies and Preparation of Standard Calibration Curve. Preparation of gallic acid- based solid lipid nanoparticles was done using spray-drying method. It was characterized for various parameters i.e., Physical appearance, Entrapment efficiency, Drug content determination, pH determination, Determination of particles size & PDI, SEM analysis, In vitro drug release and Stability studies. Gallic acid was found partial soluble in distilled water and soluble in Tween 80 and Span 20, ethanol and DMSO. Both stearic acid and cholesterol dissolved it sparingly. After 6 hours, F3 and F4 showed % drug release as 96.4±0.2, 93.2±0.5 %, respectively. Maximum release was found in F3. In conclusion, among the several forms of solid lipid nanoparticles of gallic acid, F3 demonstrated the most significant formulation i.e., in-vitro drug release, droplet size, and drug content. It also showed improved stability, with no significant change in pH, % drug release and physical appearances after being stored for 30 days. Gallic acid is promising natural moiety with a wide range of potential health benefits. Gallic acid solid lipid nanoparticles can be utilized as anti-fungal or anti-bacterial agent with sustained release.

Keywords: *Solid Lipid Nano-particles, Gallic acid, preformulation, in-vitro drug release.*

1. INTRODUCTION

Nanoparticles are solid particles having a size b/w 10-1000nm. To entrap/ attach the drug, a nanoparticle matrix is used. Biodegradable nanoparticles, especially those wrapped in hydrophilic polymers such as polyethylene glycol [1][2]. Nanoparticles are appealing for such applications because of their valuable & unique features i.e., surface to mass ratio which is greater than other particles and allowing for catalytic reaction with power to adsorb other compounds [3].

The medication is encased in polymeric nanocarriers in a spherical polymeric matrix. Polymer-based particles made of poly are a nice example. On the other hand, various forms of nanoparticles have been investigated for medical targeting. For instance, dendrimers are now being created. However, because most modern polymeric nanocarriers are biodegradable and have a reducing surface area, significant adjustments to the Higuchi equation are necessary. Furthermore, it has been proposed that solvation of the pharmacological treatment is more significant than diffusion [4]. One of the innovative prospective colloidal carrier systems for parenteral nutrition that is identical to an oil-in-water emulsion is made of solid lipid nanoparticles, which are one of the novel potential alternatives to polymers. They have various benefits, including good biocompatibility, minimal toxicity, and improved delivery of lipophilic medicines by solid lipid nanoparticles and a physically stable system [5].

Gallic acid or 3,4,5-trihydroxybenzoic acid is one of the most abundant phenolic acids in the plant kingdom. It is a colourless or slightly yellow crystalline compound, with extensive application in the food and pharmaceutical industries. Gallic acid has been isolated from different plant species such as *Quercus* spp. and *Punica* spp., via various chromatographical methods; however, from the industrial point of view, gallic acid is produced through the hydrolytic breakdown of tannic acid using a glycoprotein esterase, namely tannase [6].

Gallic acid and its derivatives such as lauryl gallate, propyl gallate, octyl gallate, tetradecyl gallate, and hexadecyl gallate, can inhibit the oxidation and rancidity of oils and fats ascribed to their free radical scavenging and antioxidant nature.

Therefore, they can be useful as additives in the food industry. Besides the edible uses of gallic acid and its ester derivatives as flavoring agents and preservatives in the food industry, there are diverse scientific reports on biological and pharmacological activities of these phytochemicals, with emphasis on antioxidant, antimicrobial, anti-inflammatory, anticancer, cardioprotective, gastroprotective, and neuroprotective effects [7].

2. MATERIALS AND METHODS

Experimental requirements

Gallic acid was purchased from the Oxford Lab Fine Chem LLP, India. Stearic acid, Span 20, Tweens 80 (Sigma Aldrich, India), distilled water, ethanol were procured from the local chemical shop in Haridwar, UK.

Table 4.1 List of chemicals and their manufacturers

Ingredients	Use	Source
Gallic acid	Active ingredient	Oxford Lab Fine Chem
Cholesterol	Polymer	SD Fine Chemicals
Stearic acid	Polymer	SD Fine Chemicals
Span 20	Plasticizer	SD Fine Chemicals
Tween 80	Plasticizer	SD Fine Chemicals
Methanol	Solvent	SD Fine Chemicals

Table 4.2 List of instruments and their manufacturers

Instruments	Model	Manufacturer
Melting point apparatus	-	Scientech
Digital weight balance	CX 220	Citizen scale
Magnetic stirrer	-	Scientech
DSC	Jade DSC	Perkin Elmer, USA
Ultrasonicator	DP120	PCI
SEM	LEO 435 VP	SEM, Cambridge
FTIR	FTIR-8400SCE	Shimadzu Corp.
Zetasizer	-	Malvern, Ltd
UV Spectrophotometer	UV-1800	Shimadzu

Preformulation studies [8][9][10].

Organoleptic properties

The purchased gallic acid was observed for its physical characteristics like colour, odour, texture of drug and compared with as reported in official monograph.

Melting point

The melting point equipment was used to determine the melting point of gallic acid. The capillary tube was filled with a small amount of gallic acid by tapping it on the drug bed, connecting it to the graduated thermometer, turning on the device, and checking for the melting point of gallic acid.

Solubility

Gallic acid was tested for solubility in surfactants. The gallic acid was added in excess to vials designed to hold 2ml of surfactant. Following vial capping, the surfactant was agitated on a vortex shaker for 24 hours, occasionally being interrupted by the shaking process. Thus, solubility was estimated in different solvent systems at room temperature.

Drug excipients compatibility studies

To validate if any changes in the drug's chemical composition following its combination with the excipients/polymers. Gallic acid was mixed with potassium bromide was applied and pressed into the shape of a disc. The disc was examined using Shimadzu FTIR spectroscopy (4000-400^{cm-1}).

Preparation of Standard Calibration Curve

The standard stock solution was prepared by dissolving 10mg of gallic acid with 10ml of methanol to give a 1000µg/ml concentration. To develop stock II, which has a concentration of 100µg/ml, take 1ml of this stock solution and diluted it with methanol (solvent) up to 10ml. A 10ml volumetric flask was filled with 1ml of the stock solution (100µg/ml), and the line was then filled with ethanol to a volume equal to 10µg/ml. The sample was then scanned with a UV-Visible spectrophotometer in the 200-400nm wavelength range using methanol as a blank. Further dilutions of 2µg/ml, 4µg/ml, 6µg/ml, 8µg/ml, 10µg/ml, and 12µg/ml were made from the stock solution (100µg/ml). The absorbance of the dilutions was measured at absorption maxima. The calibration curve was then constructed [11].

Preparation of gallic acid- based solid lipid nanoparticles

The spray-drying method was used in the formulation of SLN. Gallic acid was added and swirled until completely dissolved after the lipid components- stearic acid & cholesterol melted at 60ºC. Tween 80 and Span 20 were dissolved in distilled water to develop aqueous phase. Water that had been deionized was heated to the same temperature with constant stirring. Using homogenizer, the aqueous phase was mixed with the lipid phase for 5 min at a speed of 10,000 rpm. After that, a ultra-sonicator was used to sonicate the suspension for 5 minutes. The nanosuspension was finally cooled to room temperature.

Table 1. List of composition for the development of gallic acid- based solid lipid nanoparticles

Formulation	Gallic acid (mg)	Stearic acid (mg)	Cholesterol (mg)	Tweens 80 (%)	Span 20 (%)	Deionized water (ml)
F1	100	200	0.2	2	1	100
F2	100	300	0.2	2	1	100
F3	100	400	0.2	2	1	100
F4	100	500	0.2	2	1	100
F5	100	600	0.2	2	1	100
F6	100	700	0.2	2	1	100

Characterization parameters [12][13][14]

Physical appearance

The formulated gallic acid- based solid lipid nanoparticles were determined for their physical appearance, and color.

Analysis of particle size & PDI

The average globule size of solid lipid nanoparticles of gallic acid (Malvern Instrument) was measured using the Zetasizer Nano ZS. The intensity of the scattered light was verified to be within the sensitivity range of the device by taking measurements at a 90º angle at a temperature. At 25°C, all measurements were taken. The PDI of the formulation was determined using the same tool. The polydispersity index showed the width of the size distribution.

Entrapment efficiency

The centrifugation technique was used to calculate the entrapment efficiency of solid lipid nanoparticles of gallic acid. Methanol was used to make suspension of SLN, which was subsequently centrifuged using a high-speed cooling centrifuge (10,000rpm) for 30 min at -4ºC. The supernatant was taken-out, and the amount of free SLN was determined using UV visible spectrophotometers at 328 nm and 366 nm, respectively.

Drug content

To guarantee that the medication was released from its entrapment in the medium, a predetermined amount of SLN dispersion (200 mg) was added to a volumetric flask, suspended in methanol, and continuously shaken for 30 min. This solution was put into a centrifuge tube, spun for 15 minutes at 20°C at 12000 rpm. After being diluted with enough methanol, the supernatant filtered-off through a 0.45um membrane filter. UV-VIS Spectrophotometer, Shimadzu Japan 1601, was used to measure the concentration of the gallic acid in the supernatant at 299.5 nm and 238 nm, respectively.

Estimation of surface pH

The procedure of evaluating SLN must include calculating pH. The excipients used in the formulation control the final preparation's pH, which has an impact on the route of administration. The formulation's pH was measured using a digital pH monitor. The findings were taken in three copies to reduce error.

DSC

Additionally, it provides information on the creation of new substances and drug-excipient compatibility. As a purge gas, dried nitrogen was employed. As per usual practise, the apparatus was calibrated for heat flow and heat capacity using indium. Every sample was heated to a temperature between 25 and 300ºC at a rate of 5ºC per minute. Flow of N_2 was kept at 5ml per minute.

SEM analysis

It was employed in the analysis of film structure. Samples were placed on round brass stubs (12mm in width) using double-sided adhesive tape before being inspected by a scanning electron microscope. After 8 minutes of sputter coating at 1.1 LV in an argon environment, the samples were gold-palladium coated. Black and white Ilford PANF 50 film was used for the photography.

In-vitro drug release

A little amount of the SLN is dissolved in the PBS solution when its pH is 7.4. The solvent ethanol is then added to make the polymer soluble (pH 7.4), and the residual volume is then increased to 100 ml with PBS. After that, 1ml of the solution is removed and diluted a second time up to 10ml. The solution's absorbance is calculated at a wavelength of 270 nm, and its concentration is computed.

A modified Franz diffusion cell was used for the in vitro diffusion testing. The diffusion cell was a 10-centimeter-tall glass cylinder with a 3.7-centimeter-outside diameter and a 3.1-centimeter-inside diameter. To create a diffusion cell, a shep mucosa was attached to the cylinder at one end. A cell was treated with 1 mL of the nano emulsion and then placed in the receptor section of a beaker containing 100 mL of pH 6.8 phosphate buffer. The receptor compartment was in touch with the entire cell surface, and it was kept at 37 degrees Celsius while being magnetically agitated. To keep the sink condition constant, 10 ml of samples from the receptor compartment were removed and replaced with the same volume.

Stability profile

For 1 month, stability tests on the final optimised SLN dispersion were conducted in sealed aluminium collapsible tubes at three distinct temperatures- 5°C, 25°C, & 40°C while being periodically assessed for percent drug content, pH, texture, and other physical parameters.

3. RESULTS AND DISCUSSION

Pre-formulation studies

Melting point

The melting point of gallic acid was observed as 265°C which was found in the range of Gallic acid (reference) as 265°C. Below table refers the melting point observed:

Table 2. Melting point of Gallic acid

Drug	Reference	Sample
Gallic acid	250-265°C	265°C

Solubility

The solubility profile of gallic acid was determined in different various solvents. Gallic acid was found partial soluble in distilled water and soluble in Tween 80 and Span 20, ethanol and DMSO. Both stearic acid and cholesterol dissolved it sparingly. It was found soluble in. Gallic acid also reported good solubility in DMSO. Thus, it suggests that gallic acid is more soluble in a lipid/organic environment than in aqueous.

Table 3. Solubility of Gallic acid

Solvent	Gallic acid
Distilled water	Partial soluble
Stearic acid	Freely soluble
Cholesterol	Freely soluble
Tween 80	Soluble
Span 20	Soluble
Ethanol	Soluble
DMSO	Soluble

Drug-excipients compatibility study

Drug-excipient compatibility study was also conducted on gallic acid utilizing FTIR spectroscopy for single gallic acid and in combination with different excipients.

The following is a log and demonstration of this compatibility:

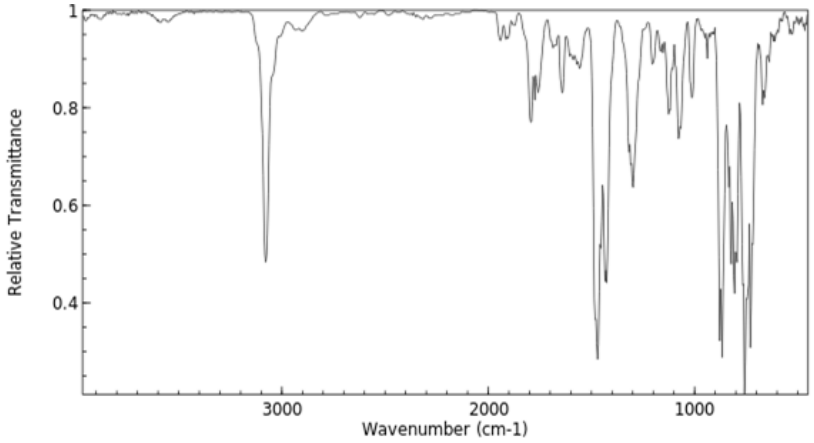


Fig 1. FTIR spectrum of Gallic acid

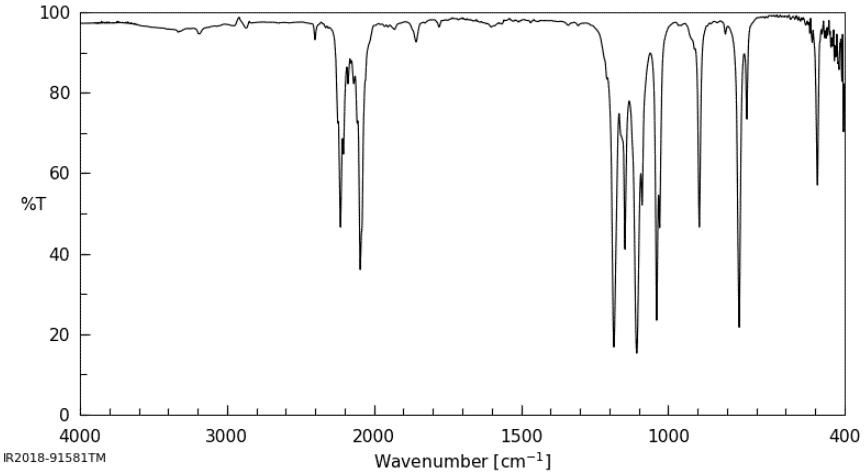


Fig 2. FTIR Spectrum of Gallic acid + Stearic acid

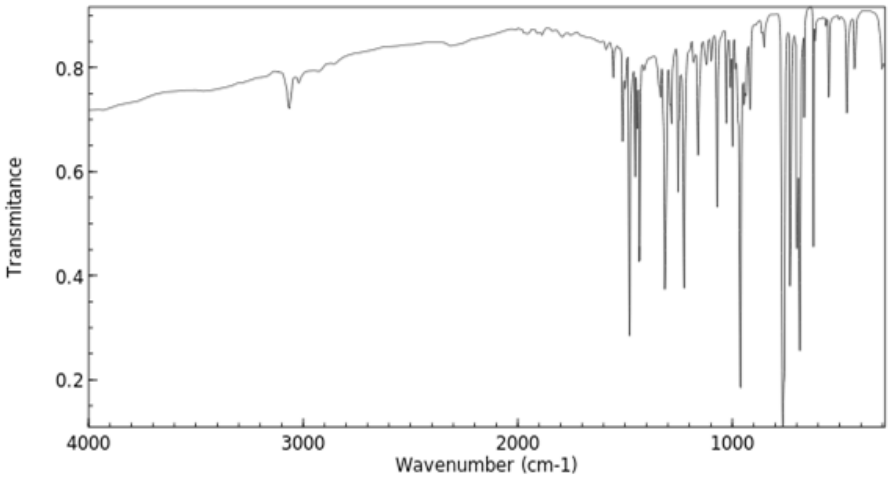


Fig 3. FTIR Spectrum of Gallic acid + Tween 80

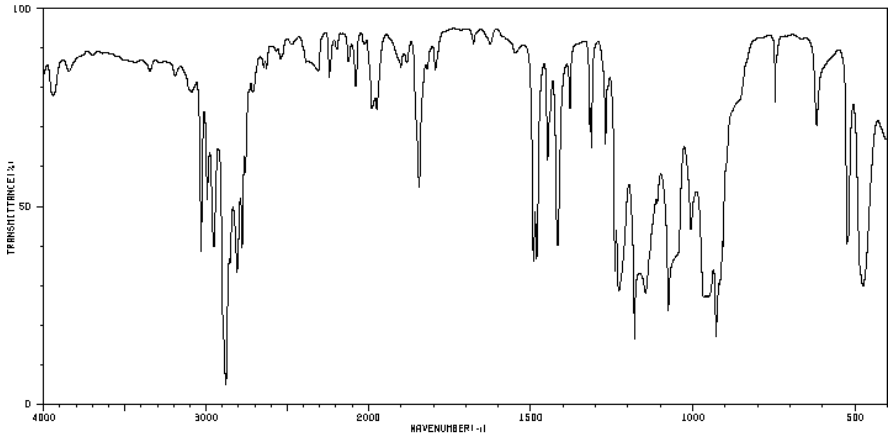


Fig 4. FTIR Spectrum of Gallic acid + Span 20

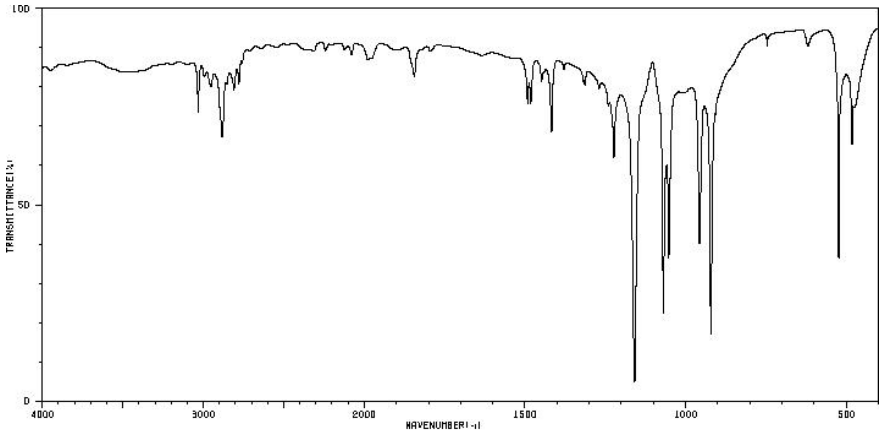


Fig 5. FTIR Spectrum of Gallic acid + Cholesterol

Standard Calibration Curve

Gallic acid was analysed using UV spectrophotometry. At 270nm, in phosphate-buffered saline (pH 7.4) containing a small amount of methanol, the absorbance of the drug was determined. Between 2 and 10g/ml, the gallic acid standard curve in PBS at pH 7.4 was linear. Beer-Lambert's law can be seen in action here.

Table 4. Std. calibration curve of Gallic acid

Conc. (µg/ml)	Optical density (absorbance)
2	0.19
4	0.35
6	0.53
8	0.66
10	0.81
12	0.93

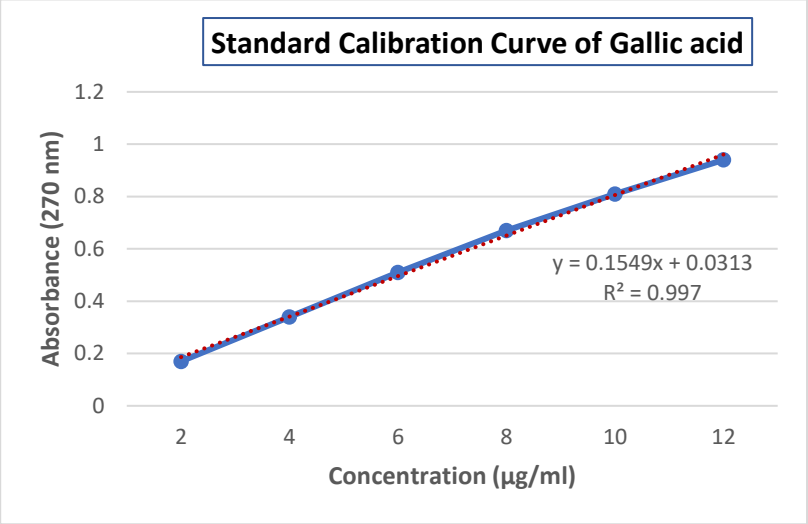


Fig 6. Standard calibration curve of gallic acid

Characterizations parameters

Physical appearance

Total 6 different types of SLNs were examined based on their outward appearances of homogeneity or heterogeneity, whiteness, and turbidity. All the formulations (F1-F6) were observed to be colourless and homogenous in appearance. This confirms for the homogenous mixing of drug with other excipients while preparation of the gallic acid- based solid lipid nanoparticles.

Table 5. Physical appearance of gallic acid- based SLN

Formulation	Physical appearance
F1	Colourless; Homogenous
F2	Colourless; Homogenous
F3	Colourless; Homogenous
F4	Colourless; Homogenous
F5	Colourless; Homogenous
F6	Colourless; Homogenous

Entrapment efficiency

Entrapment efficiency was determined as 86.21±0.19 %, 89.10±0.23 %, and 83.42±0.25 % in the F1, F3 and F6, respectively. However, the highest entrapment efficiency was found in F3 when compared with the all the other formulations. It is a special feature of solid lipid nanoparticles to characterize for the optimized formulation.

Below table demonstrates the entrapment efficiency of gallic acid- based SLN:

Table 6. Entrapment efficiency (%) of gallic acid- based SLN

Formulation	Entrapment efficiency (%)
F1	86.21±0.19
F2	79.31±0.11
F3	89.10±0.23
F4	81.27±0.30
F5	84.14±0.29
F6	83.42±0.25

Drug content

In gallic acid- based solid lipid nanoparticles, the drug content was estimated as 76.18± 0.23 %, 71.32± 0.56 %, 86.28± 0.25 %, 78.41± 0.21 %, 81.16± 0.17 % and 79.29± 0.54 % in F1, F2, F3, F4, F5 and F6, respectively. The highest drug content was reported in F3. It showed remarkable and almost identical drug content among all the formulations. These have the efficient drug release which represents the better solubility, drug-excipient compatibility etc.

Below table represents the drug content of gallic acid- based SLN:

Table 7. Drug content of gallic acid- based SLN

Formulation	Drug content (%)
F1	76.18± 0.23
F2	71.32± 0.56
F3	86.28± 0.25
F4	78.41± 0.21
F5	81.16± 0.17
F6	79.29± 0.54

Droplet size analysis

Nanodroplet analyser was utilized for the droplet size analysis of gallic acid- based SLN. It was observed as 31.15±0.45 nm, 27.34±0.23 nm, 28.20±0.28 nm, 23.16±0.23 nm, and 29.54±0.34 nm, in F1, F2, F4, F5, and F6 respectively. F3 demonstrated the lowest droplet size as 20.11±0.20 nm.

Table 8. Droplet size analysis of gallic acid- based SLN

Formulation	Droplet size (nm)
F1	31.15±0.45
F2	27.34±0.23
F3	20.11±0.20
F4	28.20±0.28
F5	23.16±0.23
F6	29.54±0.34

Analysis of PDI

The polydispersity index (PDI) estimation exhibits the particle homogeneity in topical dose formulations. The PDI values found as 0.47±0.01, 0.41±0.06, 0.43±0.04, 0.48±0.01, and 0.45±0.06 in F1, F2, F4, F5 and F6, respectively. Moreover, a lowest PDI was estimated in the F3 (0.39±0.02).

Table 9. Analysis of PDI of gallic acid- based SLN

Formulation	PDI
F1	0.47±0.01
F2	0.41±0.06
F3	0.39±0.02
F4	0.43±0.04
F5	0.48±0.01
F6	0.45±0.06

Surface pH estimation

The formulation's surface pH was measured and found to be slightly basic/acidic in F1-F6. The surface pH was estimated, 1 hour post formulation of SLN. Therefore, it might confirm that the pH range used to manufacture the solid nanoparticles was ideal for their tolerance and solubility in saliva.

Table 10. Surface pH of gallic acid- based SLN

Formulation	pH
F1	7.2± 0.14
F2	6.7± 0.23
F3	6.8± 0.15

F4	7.4± 0.27
F5	6.4± 0.20
F6	7.6± 0.12

DSC estimation

DSC analysis was performed to check that how the formulations are resistant to the moisture and increasing temperature. Formulations F1-F6 were shown almost identical response with the temperature in range of 270ºC to 285ºC.

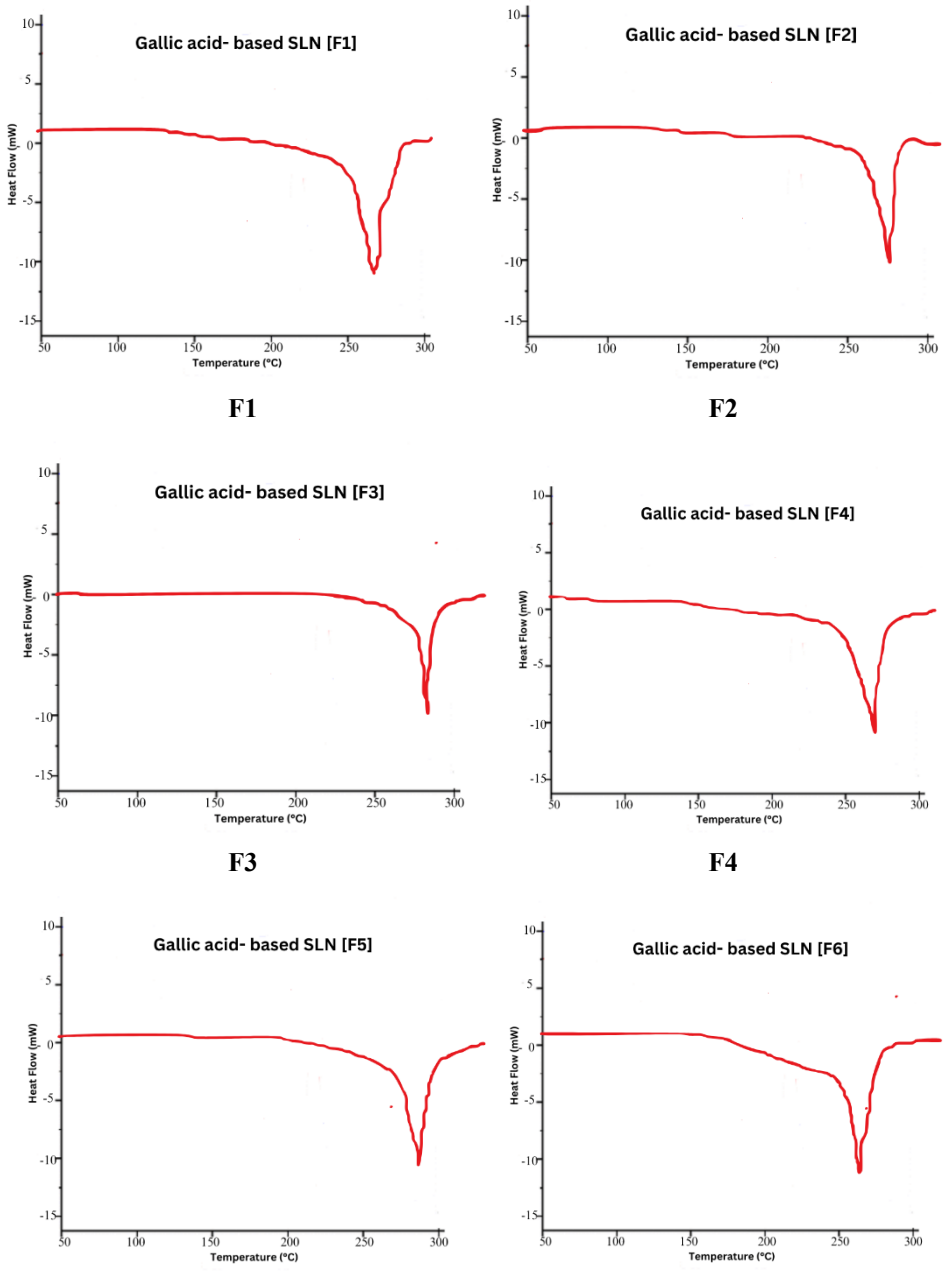
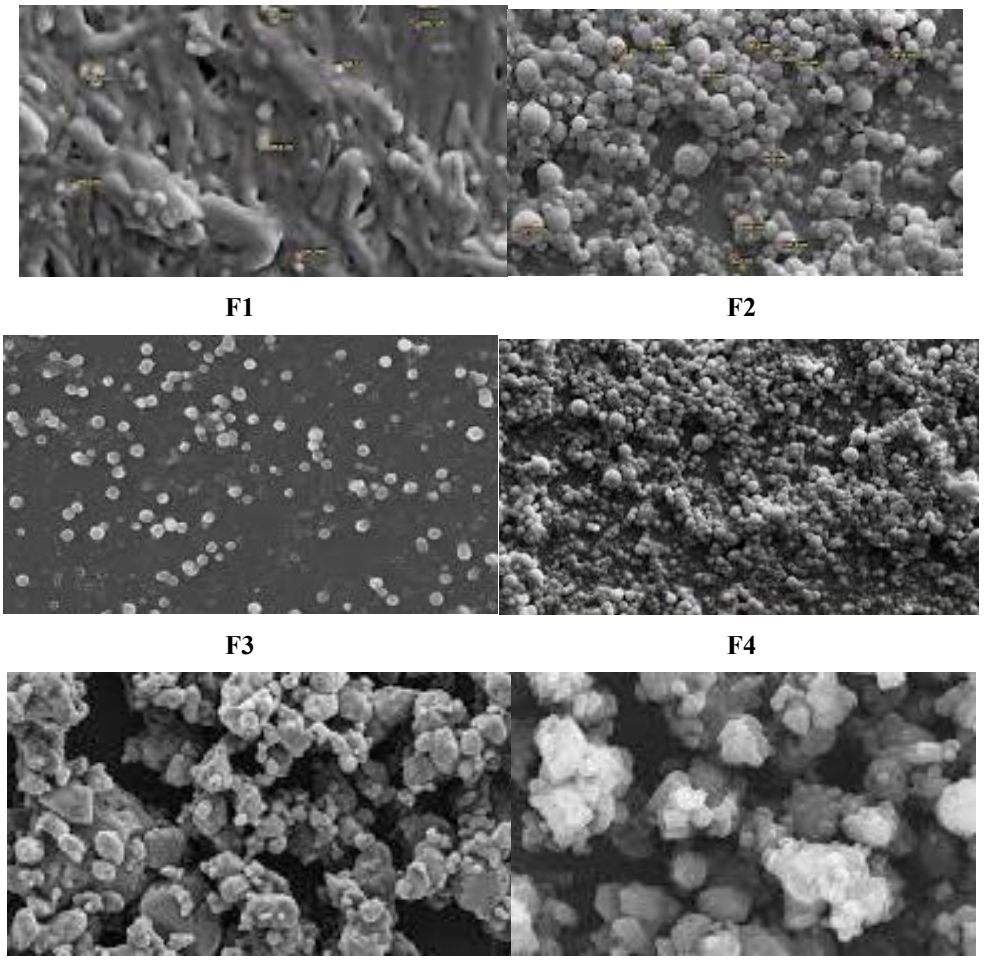


Fig 7. DSC thermographs of gallic acid- based SLN

SEM determination

All the formulations of gallic acid- based solid lipid nanoparticles were analysed for SEM. All the formulations were observed in the range of 100-1000 nm.



F1 **F2**

F3 **F4**

F5 **F6**

Fig 8. Illustration of SEM determination of gallic acid- based SLN

***In-vitro* drug release**

The in vitro drug release was estimated in the prepared SLN formulations. It was found optimistic and near to 100% so it showed an excellent stability for all the formulations. After 6 hours, F3 and F4 showed % drug release as 96.4±0.2, 93.2±0.5 %, respectively. Maximum release was found in F3.

Table 11. In-vitro drug release of gallic acid- based SLN

Time (hr)	% Drug release± S. D. F1	F2	F3	F4	F5	F6
1	29.3±0.1	31.5±0.4	34.1±0.6	33.2±0.4	28.3±0.1	30.2±0.2
2	42.2±0.6	39.4±0.1	43.3±0.2	41.6±0.2	38.8±0.2	41.6±0.5
3	57.6±0.1	55.6±0.3	58.4±0.1	52.2±0.7	53.1±0.7	59.2±0.3
4	68.3±0.2	66.1±0.1	71.3±0.4	64.1±0.3	63.6±0.3	70.1±0.4

5	80.4±0.3	78.4±0.2	84.1±0.3	76.6±0.1	78.2±0.2	81.5±0.2
6	91.2±0.4	89.2±0.4	96.4±0.2	87.2±0.4	90.4±0.4	93.2±0.5

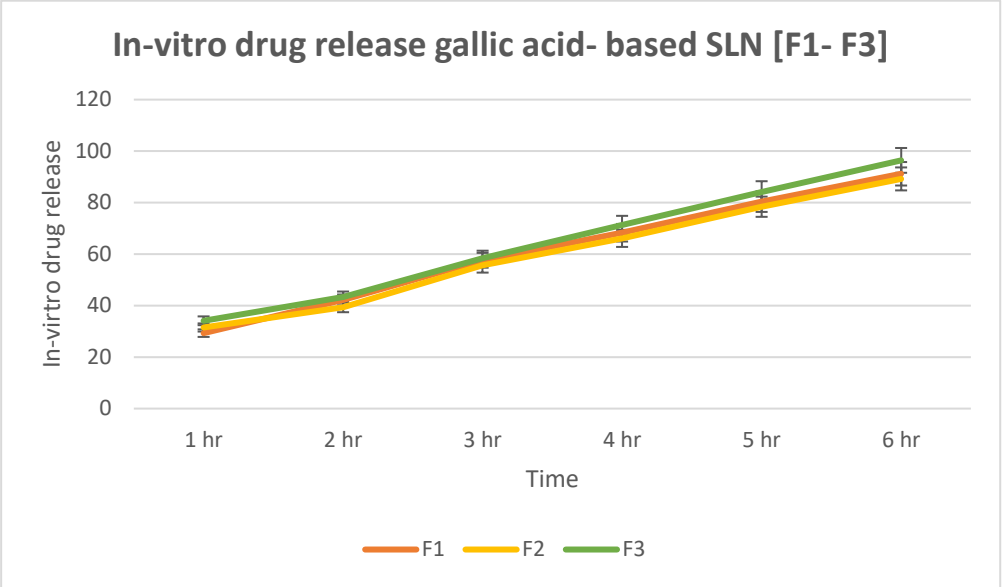


Fig 9. In-vitro drug release of gallic acid- based SLN [F1- F3]

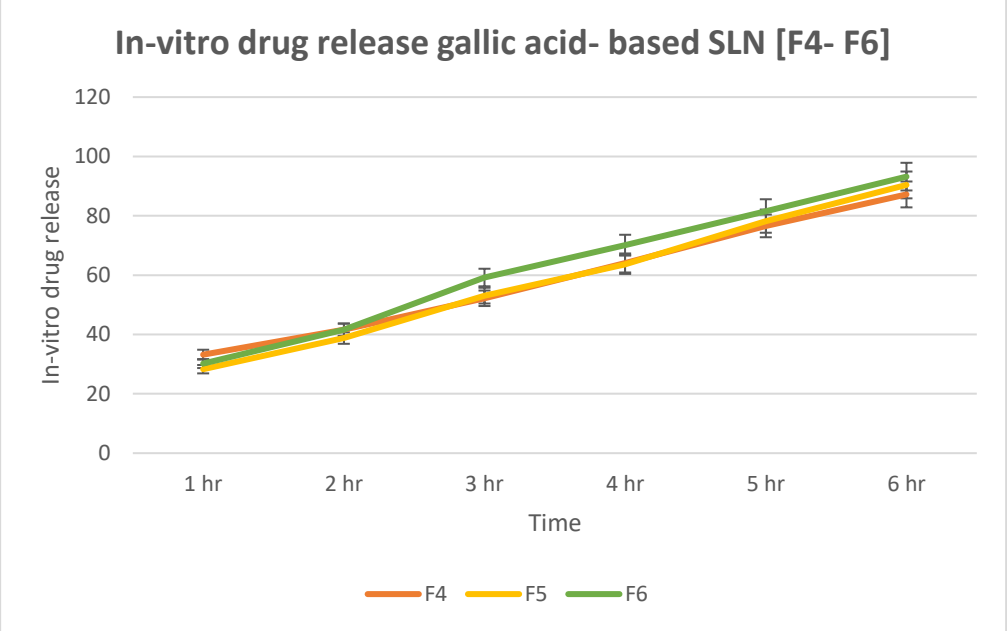


Fig 10. In-vitro drug release of gallic acid- based SLN [F4- F6]

Stability profile

To determine the stability profile of solid liquid nanoparticles, their physical characteristics were examined. After 30 days of storage, the physical characteristics of a number of solid liquid nanoparticles were found to be consistent. Therefore, it is feasible to conclude that solid lipid nanoparticles based on gallic acid that were made using these excipients were very stable and effective.

Although nanoparticles are more reactive, effective, and bioavailable than traditional drug delivery methods, their application in clinical practice still requires development. Immunogenicity and biocompatibility are the primary obstacles to creating and utilizing goods based on nanoparticles. As a result, regulatory agencies including the European Medicines Agency (EMA) and the USFDA have set standards for its efficacy, safety, toxicity, and quality. Studies have indicated that the activation of the immune complement system in response to medication delivery systems that are nanoparticularized may cause hypersensitivity reactions. The production of free radicals, which cause oxidative stress, may be one reason for the dangerous reaction of nanoparticles. When free radical concentrations are excessive, they can damage proteins, lipids, DNA, and other biological components. Furthermore, before being used in clinical settings, goods based on nanoparticles must pass stringent regulatory approval procedures [15]. The potential of drug delivery technology using solid lipid nanoparticles to improve medical treatments has not yet been completely realized. The composition, the production process's speed and efficiency, including its capacity for large-scale production, and the potential to produce carriers with improved encapsulation efficiency are all distinct benefits of SLN. The loading capacity of SLNs is decreased by partitioning effects during manufacture, which makes it challenging to give hydrophilic medications.

Therefore, after a month of storage, it can be said that the solid lipid nanoparticles made with gallic acid showed a stable formulation when tested for pH, in-vitro drug release, and physical appearance.

4. CONCLUSION

Solid lipid nanoparticles are becoming more and more popular as drug carriers for improving the delivery of pharmacological active components because they offer a few advantages for pharmaceutical delivery. They exhibit promise in a range of industries, such as biotechnology, cosmetics, and pharmaceuticals, because they can be adapted to almost any distribution strategy. The low absorption and poor miscibility of certain phytopharmaceuticals with the lipids present in cell membrane linings may be addressed by this innovative approach.

In conclusion, among the several forms of solid lipid nanoparticles of gallic acid, F3 demonstrated the most significant formulation i.e., in-vitro drug release, droplet size, and drug content. It also showed improved stability, with no significant change in pH, % drug release and physical appearances after being stored for 30 days.

Gallic acid is promising natural moiety with a wide range of potential health benefits. Gallic acid solid lipid nanoparticles can be utilized as anti-fungal or anti-bacterial agent with sustained release. The clinical trials are required to fully realize their therapeutic potential and optimize their use in various health conditions.

5. CONFLICT OF INTEREST

None.

REFERENCES

[1] Tyagi P, J.A. Subramony. Guidance for Industry: Considering Whether an FDA-Regulated Product Involves the Application of Nanotechnology, Food and Drug Administration (Accessed 02 Fig. 4. Schematic showing flexibility for developing immunotherapy combinations based on patient parameters such as tumor phenotype and tumor biomarker information. Journal of Controlled Release, 2018; 272:159-168.

[2] Liu L, Q. Ye, M. Lu, Y.C. Lo, Y.H. Hsu, M.C. Wei, Y.H. Chen, S.C. Lo, S.J. Wang, D.J. Bain, C. Ho, A new approach to reduce toxicities and to improve bioavail- abilities of platinum-containing anti-cancer nanodrugs, Sci. Rep. 5 (2015) 10881.

[3] Merisko-Liversidge E, G.G. Liversidge. Nanosizing for oral and parenteral drug delivery: a perspective on formulating poorly-water soluble compounds using wet media milling technology, Adv. Drug Deliv. Rev. 63 (2011) 427-440.

[4] Maeda H, H. Nakamura, J. Fang, The EPR effect for macromolecular drug delivery to solid tumors: improvement of tumor uptake, lowering of systemic toxicity, and distinct tumor imaging in vivo, Adv. Drug Deliv. Rev. 65 (2013) 71–79.

[5] Mukherjee S, S. Ray and R. S. Thakur, Ind. J. Pharm. Sci., 349-358 (2009).

[6] Fernandes F, Salgado H. Gallic acid: review of the methods of determination and quantification. Crit Rev Anal Chem. 2016;46:257–265.

[7] Choubey S, Varughese L, Kumar V, Beniwal V. Medicinal importance of gallic acid and its ester derivatives: a patent review. Pharm Pat Anal. 2015;4:305–315.

[8] Samiullah, Jan SU, Gul R, Jalaludin S, Asmathullah, “formulation and evaluation of transdermal patches of pseudoephedrine HCL”, International Journal of Applied Pharmaceutics, 2020,12(3), 121-127.

[9] Chauhan SB, Saini S, “formulation and evaluation of transdermal patches of metoprolol tartrate using

permeation enhancers of natural and synthetic origin", Int J App Pharm, 2019,11(5), 293-298.

[10] Kulkarni S. Formulation and Evaluation of Transdermal Patch for Atomoxetine hydrochloride. JDDT, 2019;9(2-A):32-5.

[11] Jirapornchai Suksaeree, Chomnapas Chuchote. Accelerated Stability Testing of a Polyherbal Transdermal Patches Using Polyvinyl Alcohol and Hydroxypropyl Methylcelluloseas a Controlling Polymer Layer. Journal of Polymers and the Environment (2018) 26:4056–4062.

[12] Kavitha K and More Mangesh Rajendra, Design and Evaluation of Transdermal Films of Lornoxicam, IJPBS, 2011, 2(2), 54-62.

[13] Shalu Rani, Kamal Saroha, Navneet Syan, Pooja Mathur, Transdermal Patches A Successful Tool In Transdermal Drug Delivery System: An overview, Der Pharmacia Sinica, 2011, 2 (5), 17-29.

[14] D NV, Shrestha N, Sharma J. Transdermal drug delivery system: An overview. Int J Res Pharm Sci. 2012;3(2):234–41.

[15] Kyriakides T.R., Raj A., Tseng T.H., Xiao H., Nguyen R., Mohammed F.S., Halder S., Xu M., Wu M.J., Bao S., et al. Biocompatibility of nanomaterials and their immunological properties. Biomed. Mater. 2021;16:042005.