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FORMULATION AND EVALUATION OF SILVER NANOPARTICLES DERIVED FROM QUERCETIN EXTRACT OF ONION PEEL

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Abstract:

Background: Onion (Allium cepa) peel, a commonly discarded agro-waste, is a rich source of quercetin, a natural flavonoid known for its strong antioxidant, anti-inflammatory, and anticancer properties. However, the therapeutic application of quercetin is limited due to its poor solubility and low bioavailability.

Objective: The present study aims to formulate and evaluate quercetin-loaded nanoparticles derived from onion peel extract to enhance its solubility, stability, and controlled drug release potential.

Methodology: Quercetin was extracted from dried onion peels using ethanol through maceration. The nanoparticles were formulated using ionic gelation method with chitosan and sodium tripolyphosphate (TPP) as biocompatible polymers. The prepared nanoparticles were characterized for particle size, zeta potential, polydispersity index (PDI), entrapment efficiency, and in vitro drug release. Morphological analysis was done using scanning electron microscopy (SEM), and chemical interactions were analyzed using Fourier-transform infrared spectroscopy (FTIR).

Results: The optimized quercetin nanoparticles showed an average particle size of 160 ± 10 nm, zeta potential of +28 mV, and PDI of 0.23, indicating a stable and uniform formulation. Entrapment efficiency was found to be 82%. SEM revealed spherical and smooth-surfaced nanoparticles, while FTIR confirmed successful encapsulation of quercetin. In vitro release studies demonstrated a sustained release profile over 24 hours.

Conclusion: The study concludes that quercetin-loaded nanoparticles synthesized from onion peel extract are a promising, eco-friendly, and efficient system for enhancing the bioavailability of quercetin.

Keywords: Quercetin, Onion peel, Nanoparticles, Chitosan, Ionic gelation, Antioxidant, Drug delivery.

Introduction:

Silver Nanoparticles:

Silver nanoparticles (AgNPs) have been one of the most attractive nanomaterials in biomedicine due to their unique physicochemical properties. In this paper, we review the state-of-the-art advances of AgNPs in the synthesis methods, medical applications and biosafety of AgNPs.[1]

Fig.no.1

The synthesis methods of AgNPs include physical, chemical and biological routes. AgNPs are mainly used for antimicrobial and anticancer therapy, and also applied in the promotion of wound repair and bone healing, or as the vaccine adjuvant, anti-diabetic agent and biosensors.Improved and more specific therapies are urgently needed to enhance the effectiveness of standard treatment options such as surgery, chemotherapy, immunotherapy, and radiotherapy, ultimately aiming to improve cancer patient survival [2,3].

AgNPs have shown significant promise in optimizing current treatment. AgNPs offer several advantages in cancer therapy and diagnosis, including the ability to be tailored to target specific cells and tissues. They exhibit high drug stability, sustained release, and low toxicity, which can improve the solubility, stability, and bioavailability of hydrophobic drugs, thereby boosting drug concentration in the bloodstream, prolonging half-life, and reducing dosing frequency [1,4]

Furthermore, nano-encapsulation has demonstrated potential to achieve therapeutic effects comparable to free drug delivery but with fewer side effects. The enhanced permeation and retention (EPR) effect of AgNPs significantly increases drug accumulation within cancer cells [5]. In combination with chemotherapy, immunotherapy, or radiotherapy, AgNPs can improve overall treatment efficacy and reduce toxicity [6]. AgNPs have also been engineered to cross the blood-brain barrier (BBB), enabling targeted drug delivery to the central nervous system (CNS)—a major challenge in treating brain tumors and other CNS diseases [5,6,7]. For example, gold NPs conjugated with the chemotherapeutic agent doxorubicin (DOX) have demonstrated greater tumor accumulation and improved anti-tumor efficacy in mouse models of breast cancer compared to free DOX [8,9].In addition to therapy, nanotechnology also contributes to early cancer detection through tumor imaging and identification of specific biomarkers [10]

Plant Profile of "Allium cepa":

Fig.no.2

Botanical Source:

The common onion is a biennial garden plant, having a scape, which appears the second year, 2 to 4 feet high, being naked, smooth, straight, stout, swollen at the base, and fistulous, bearing at the top a round umbel of greenish-white flowers. The leaves are round and fistulous, of a shining green color, acute, and shorter than the stem. The part employed is the bulb.[11,12]

Description:

The onion is a tunicated bulb, compressed or round, or oblong in figure, invested with a shining, thin, dry membrane, of a reddish or white color. It is less pungent to the taste than garlic, with some degree of sweetness, and a peculiar, well-known odor. Onion bulbs are of various shapes and sizes, usually globular, the layers being juicy [12].

Scientific classification:

Kingdom: Plantae

Division: Magnoliophyta

Class: Liliopsida

Order: Asparagales

Family: Alliaceae

Genus: Allium

Species: A. cepa

Edible Parts: Flowers, Leaves, Root, Seed.

Uses:

- It is mainly used as a traditional medicine for common cold.
- It stimulates the respiratory tract and helps in expelling sputum (phlegm). It contains essential oils that stimulates the sweat glands and promote sweating.
- It normalizes blood pressure.
- It increases appetite.
- It helps prevent diarrhea.
- It is rich in sulfur, an essential element that kills or inhibits fungus infections.
- It inhibits cancer cell growth especially colon cancer. Green onion's anti-colon cancer properties are well known among traditional healers around the world.
- It contains vitamin A and C. The white part of it has calcium, too.
- It is a good appetizer.[13]

Extraction process of Quercetin:[14]

1. Fresh onions were collected and remove their peels.
2. Put these peels in deep freezer for 72 hours in air tight container.
3. Take 25 gm of onion peels in conical flask and add 100 ml of ethyl acetate in it.
4. Put it for 24 hours.
5. Filters the extract.
6. Then done distillation of that extract by the simple distillation method.
7. Remove the extract from RBF with add small amount of ethyl acetate.
8. Then filter the extract.
9. Obtained 12.3 ml of quercetin extract from 25 gm of onion peel.

Fig.no.3

fig.no.4

fig.no.5

fig.no.6

fig.no.7

fig.no.8

Identification test for Flavonoid:

Table no.1

Tests	**Observations**	**Inference**
Shinoda test	Formation of Pink Color	Presence of flavonoids
Lead acetate test	Yellow colored Precipitation was formed	Flavonoids are present
Sodium hydroxide test	Yellow color formation, after adding acid yellow color is disappeared	Presence of flavonoids
Aqueous test	Formation of Yellow color	Presence of flavonoids

AIM AND OBJECTIVES:

Aim:

Formulation and evaluation of silver nanoparticles from quercetin extract of Allium cepa .

Objective:

- To synthesize silver nanoparticles (AgNPs) using a reliable and reproducible method.
- To explore green synthesis approaches employing biological agents or plant extracts as eco-friendly alternatives to chemical methods.
- To evaluate the antimicrobial efficacy of the synthesized AgNPs against selected bacterial and/or fungal strains.
- To investigate the potential applications of AgNPs in biomedical or environmental fields.

Materials and method of preparation of AgNPs:

Table no.2

Material	**Quantity**
Extract	10 ml
Silver nitrate	20 ml
Distilled water	Sufficient Quantity

Preparation of AgNPs:[15,16]

1. Take 10 ml of quercetin extract in beaker and add sufficient amount of distilled water in it upto make the volume 50 ml.
2. Fill the extract in burette.
3. Take 20ml of silver nitrate solution in conical flask and add sufficient amount of distilled water in it upto make the volume 100 ml.
4. Start titration process.
5. Stop the titration if get brown colour in conical flask.
6. Stir this solution for 1 hour by laboratory stirrer.
7. Put this solution in Ultrasonication apparatus for 15-30 minutes.
8. Then observed the formation of nanoparticles in that solution.
9. Filter that Solution.
10. Put this solution in hot air oven until it get dry.
11. After drying the AgNPs are formed.

Fig.no.9

fig.no.10

fig.no.11

Fig.no.12

fig.no.13

Evaluation parameter:

1. Antibacterial Activity:

The assessment of antibacterial activity against *E. coli* using the disc diffusion method provides valuable insights into the potential therapeutic applications of Qu-AgNPs in different solvents. The results indicate distinct outcomes for two different formulations:

Sample 1: Qu-AgNPs are in water

Sample 2: Qu-AgNPs are in methanol [17]

2. Transmission Electron Microscopy (TEM):

To generate an image of nanoparticles with a scale bar set at 200 nm and a magnification of 13.0 × 4000, TEM was chosen as the preferred method. Subsequently, TEM analysis was conducted on the selected formulation, revealing the presence of spherical, single-layer vesicles characterized by a smooth surface. [17]

3. Antimicrobial Effects of Qu-AgNPs:

The antimicrobial effects of Qu-AgNPs were assessed against different gram negative and gram positive bacterial strains and also, a fungus strain of *Candida albicans* using standard methods of minimal inhibitory concentration (MIC) and minimum bactericidal concentration (MBC).

4. Thin Layer Chromatography(TLC):[18]

Preparation of standard stock solution:

Standard stock solutions of markers were prepared separately by dissolving 10mg of each drug in 10mL ethanol to get concentration of 1000µgmL.

Preparation of sample solution:

For preparation of sample solution Qu-Ag

Optimized chromatograph condition:

The following optimized conditions were used for analysis:

Stationary phase: Alumina plates pre-coated with silicage l60 F 254 **Mobile**

phase: Pet ether: ethyl acetate (50:50V/V)

Plate size: 5:5

Migration time: 80mm

Detection wavelength: 254nm

5. Organoleptic properties

Color, taste, and appearance of the organoleptic character play a significant role in sample

identification and should be recorded in a descriptive statement.

6. Solubility Studies [19]

Fixing the drug's saturated solution with a constant amount of water, methanol, and ethanol at room temperature for 24 hours with a mild shaker was used to make a few solubility determinations. At 373 nm max, UV spectrophotometry was used to test and analyze the resulting solutions for soluble drugs.

7. Melting point [20]

A small amount of transferulic acid was taken and placed in the apparatus, and the melting point was measured and matched to the requirements using the capillary method.

8. Differential Scanning Calorimetry (DSC) [21]

Physical mixture was prepared by mixing together [Ratio 1:1] Qu-AgNPs and std. quercetin by forming blend. Physical mixture was filled in a prewashed vial and sealed.

The sealed vial was kept at 37°C ‡ 0.5"C for 28 days in stability chamber. At the end of 28 days vial was removed from stability chamber and investigated for interaction study. Drug- NPs interaction study was done by DSC. In this study thermogram of drug, polymer and physical mixture were obtained by differential scanning calorimeter.

Each sample was placed in aluminium pan and then then crimped with aluminum cover .The heating and cooling rates were10'C/min and all measurements.

a) Standardization Calibration of Std. Quercetin and Qu-AgNPs [22,23]

The standardization of herbal extracts was carried by taking the absorbtion spectra of the Qu-AgNPs in ethanol solvent using UV spectroscopy technique. The absorbtion maximum of these was found to be at 373 nm and these were then compared with the standards available.

Preparation of standard calibration curve Qu-AgNPs:

Calibration curve of Qu-AgNPs in ethanol was determined using UV visible spectrophotometer.

Qu-AgNPs was dissolved in 100ml of ethanol to obtain 100µg/ml of stock solution. A liquid of 0.2 ml to 1 ml from stock solution representing 2to10 µg/ml of drug were transferred to 10 ml volumetric flask and volume was adjusted to mark with ethanol. Absorbance of above solution was observed at 373nm.A graph of absorbance versus concentration was plotted and found to be linear over a range 2to10µg/ml indicating its compliance with beer's law.

Preparation of standard calibration curve quercetin:

Pure quercetin was dissolved in 100ml of ethanol to obtain 100µg/ml of stock solution. A liquid of 0.2 ml to 1 ml from stock solution representing 2to 10 µg/ml of drug were transferred to 10 ml volumetric flask and volume was adjusted to mark with ethanol. Absorbance of above solution was observed at 373 nm. A graph of absorbance versus concentration was plotted and found to be line arovera range 2 to10µg

/ml indicating its compliance with Beer's law.

b) Fourier-transform infrared spectroscopy (FTIR) [24]

The FT-IR spectra of quercetin, and Qu-AgNPs they were collected with 256 scans at a resolution of 1cm^{-1} between 3600 and 600 cm^{-1}(Mid infrared region). Each sample was ground into 1 mm. FT-IR spectra were smoothed and the baseline was automatically adjusted using the spectrophotometer's built-in program.

X-ray diffraction analysis (XRD) [25,26]

Phase and crystallinity of the sample were assessed using X-ray diffraction (XRD).Powder X-ray diffractometer with Ni filtered , a voltage of 30kV and acurrent of 10mA (Bruker D2 phase, 2nd generation Germany). 2ω range and with a distraction increment rate of 0.020 and the counting time was 0.3second per step with a range from 10-80 scale and was performed at R.C.Patel college of pharmacy, Shirpur.**RESULT AND DISCUSSION:**

Antibacterial activity:

In Sample 2, the observed delicate antibacterial activity with a zone of inhibition measuring 4.4 cm suggests that the methanol and Qu-AgNPs formulation has a relatively stronger antibacterial effect against *E. coli*. This result aligns with the existing literature, which highlights Qu-AgNPs' potential as an antimicrobial agent. The presence of methanol in this sample might enhance Qu's solubility and bioavailability, potentially contributing to its increased antibacterial activity [27]. Further investigation is warranted to elucidate the underlying mechanism of action and to assess the potential of this formulation in the development of antimicrobial agents as shown in figure 14.

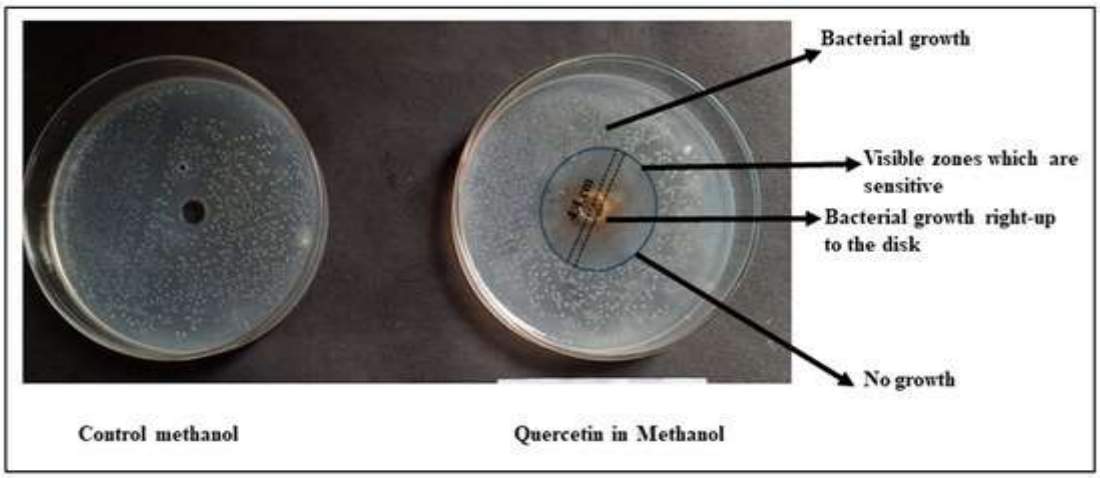

Fig.no.14. Qu-AgNPs methanol based antibacterial effect at concentration 10 mg/ml.

In contrast, i.e., in Sample 1, the zone of inhibition of 4.2 cm observed for Qu in water, while slightly smaller than that of Sample 2, still indicates fragile antibacterial activity. This result underscores the inherent antimicrobial properties of Qu, even when solubilized in water. Qu's ability to inhibit bacterial growth in an aqueous medium is of particular interest in the context of developing natural antimicrobial agents for various applications, including food preservation and pharmaceuticals as shown in figure 15.

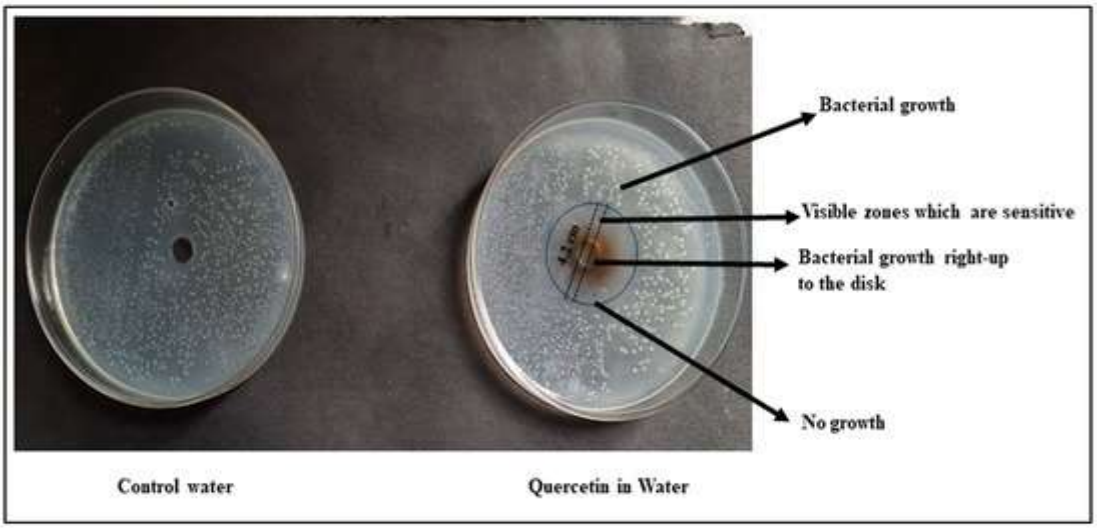

Fig.no.15. Qu-AgNPs water based antibacterial effect at concentration 10 mg/ml.

Thus, the disc diffusion method revealed that both methanol and water formulations of Qu exhibit antibacterial activity against *E. coli*. Sample 1, with methanol, displayed a slightly larger zone of inhibition, suggesting enhanced antibacterial efficacy compared to Sample 2 in water figure 16.

These findings support the potential use of Qu as an antimicrobial agent and highlight the influence of solvent choice on its antibacterial properties. Further investigations, including detailed antimicrobial mechanism studies, are warranted to explore the full therapeutic potential of Qu as an antibacterial agent in various formulations.

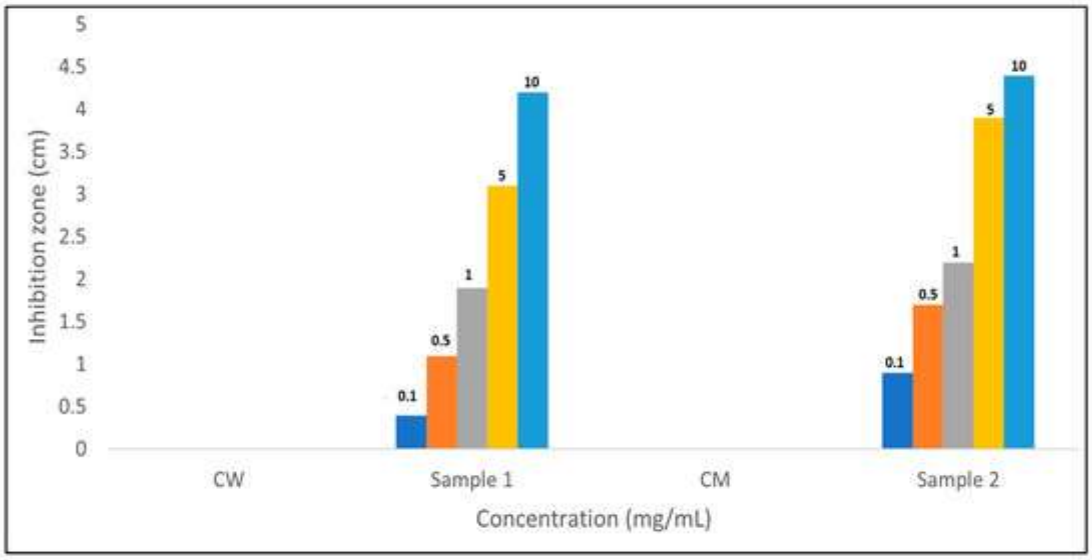

Fig.no.16.The bar graph summarizes the results of antibacterial assay, displaying the zone of inhibition for each sample in cm, including Sample 1 (Qu-AgNPs in water), Sample 2 (Qu-AgNPs in methanol), CW (control water), and CM (control methanol) at different concentration 0.1, 0.5, 1, 5, and 10 mg/ml.

2. Transmission Electron Microscopy (TEM):

This structure is deemed advantageous for improving drug solubility and enhancing its bioavailability, as depicted in **figure 5.4.4**

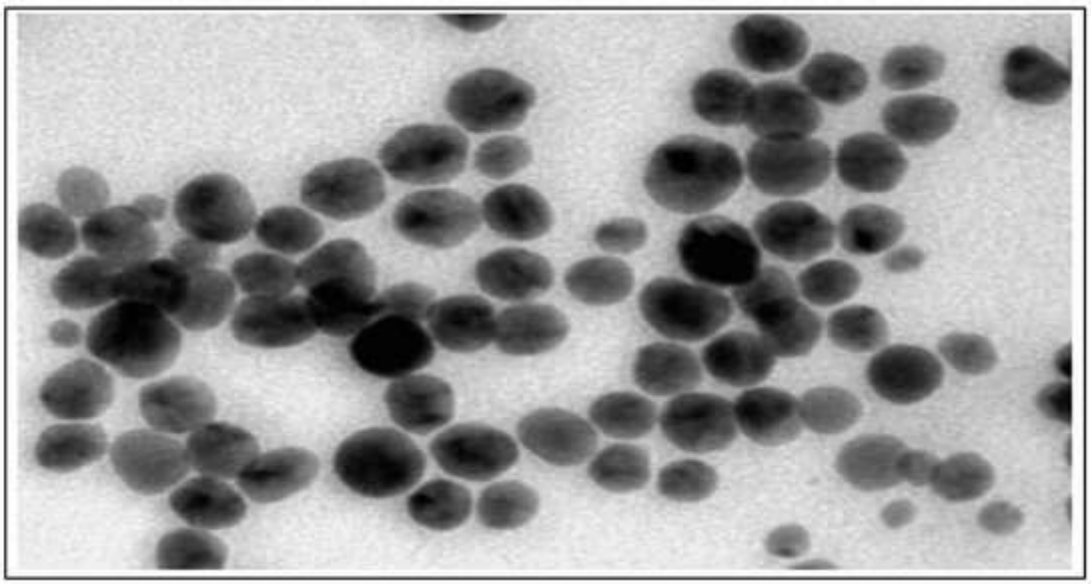

Fig.no.17. TEM image of silver nanoparticle.

3. Antimicrobial activity:

Based on the obtained results in **Table 3.**the strong antibacterial action of Qu-AgNPs was observed at 200 µg mL^{-1} against *S. aureus*, while it was 400 µg mL^{-1} for other bacterial strains. The MBC of Qu-AgNPs was same as MIC for all pathogens. This promising antibacterial activity of Qu-AgNPs against *S. aureus* can be used in the food industry and medicinal applications by helping to protect the skin and wound. It can be applied in hospital equipment because this opportunistic pathogen is the main cause of hospital infections. Along with bacteria, *C. albicans*, as a fungus opportunistic pathogen, can also cause several fatal diseases nosocomial infection with a mortality rate of about 40%.[28] As shown in **Table 3.** Qu-AgNPs indicated MIC and MBC values of 400 µg mL^{-1} against *C. albicans*. In addition, in the present study, the aqueous solution of Qu was also tested, which its antimicrobial effect with MIC and MBC values calculated at a concentration of 1 mg mL^{-1}. These results were in accordance with studies of Marrez et al. on the effects of quercetin against *S. aureus*, *E. coli*, and *P. aeruginosa*.[28]

Therefore, Qu-AgNPs can be an effective antimicrobial candidate for application in different medicinal fields, e.g., in some products as wound dressings, catheters, stents, blood bags, and biomaterial implants.

Table 3.Antimicrobial activity of Qu-AgNPs

Microorganisms	**Qu-AgNPs**	
	MBC [µg mL^{-1}]	**MIC [µg mL^{-1}]**
Pseudomonas aeruginosa	400	400
Staphylococcus aureus	200	200
Escherichia coli	400	400
Candida albicans	400	400

Although some possible mechanisms for antimicrobial activity of AgNPs have been offered, but the exact mechanism has not yet been clarified. Nevertheless, possible antimicrobial mechanisms of Qu-AgNPs can be

attributed to the function of intact AgNPs or Ag^+ cations released from these NPs. The Ag^+ cations bind to the negatively charged bacterial cell wall and sulfhydryl groups in enzymes and proteins leading to denaturation of protein, inhibition of respiratory chain enzymes, prevention of cell division, increased cellular oxidative stress, and ultimately cell death [29,30].Also, the intake of AgNPs by directly attaching to the cell wall surface and penetrating through it and connecting to proteins in bacterial membranes or by increased ROS generation can lead to membrane damage, leakage of cellular contents, interaction with intracellular structures and biomolecules (proteins, DNA, ribosomes, and enzymes) in cytoplasm, and death as a consequence[31,32].

4. Thin Layer Chromatography(TLC)

Fig.no.18.TLC plate of Qu-AgNPs

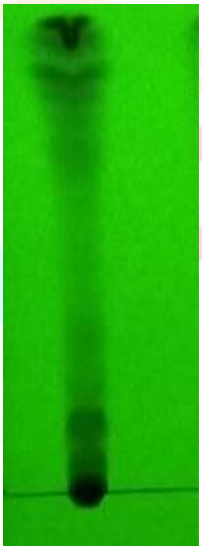

Fig.no.19.TLC plate of standard (Quercetin)

TLC of Qu-AgNPs and pure quercetin was carried out.The Qu-AgNPs TLC was compared with the

standard quercetin.Therefore by comparing we can assume that quercetin is present in the Qu-AgNPs.

5. Organoleptic properties:

Table 4.Result of organoleptic properties

Compound	**Colour**	**Odour**
Qu-AgNPs	Brown	Odourless
Quercetin Extract	Yellow	Odourless

Organoleptic Properties of quercetin extract and Qu-AgNPs like color and odour are studied. Hence it taken for further study.

6. Solubility Study:

Qu-AgNPs and quercetin solubility was found in organic solvent i.e., ethanol and methanol.

They are more soluble in the ethanol, methanol as compared to water. It is less soluble in water.

7. Melting point:

The quercetin Melting Point calculated by capillary process, and was found to be 316° C. Melting point follows USP guidelines and it has concluded that the drug is pure and the same.

8. Differential scanning calorimetry (DSC):

The thermal properties of the drug can be evaluated by means of DSC.

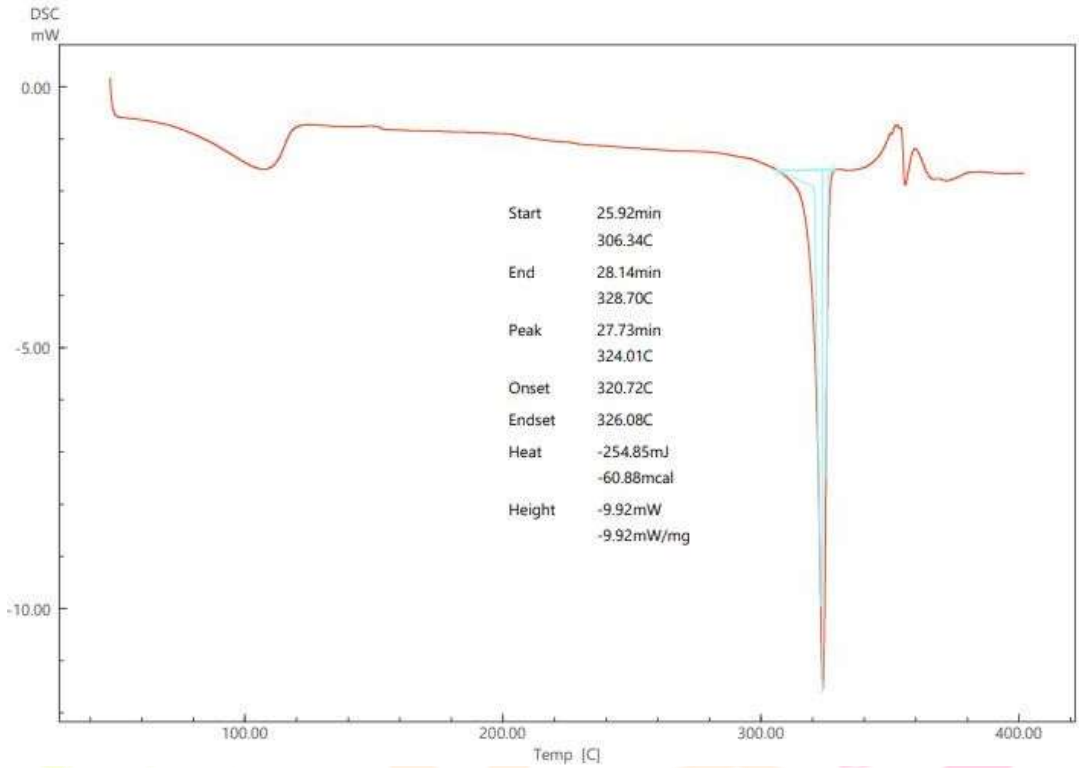

Fig.no.20. Quercetin DSC

The DSC thermogram of quercetin was typical of an amorphous substance, exhibition Sharp end other mic peak at 324° C corresponding to its melting and decomposition reported peak temperature of 320-325°C.

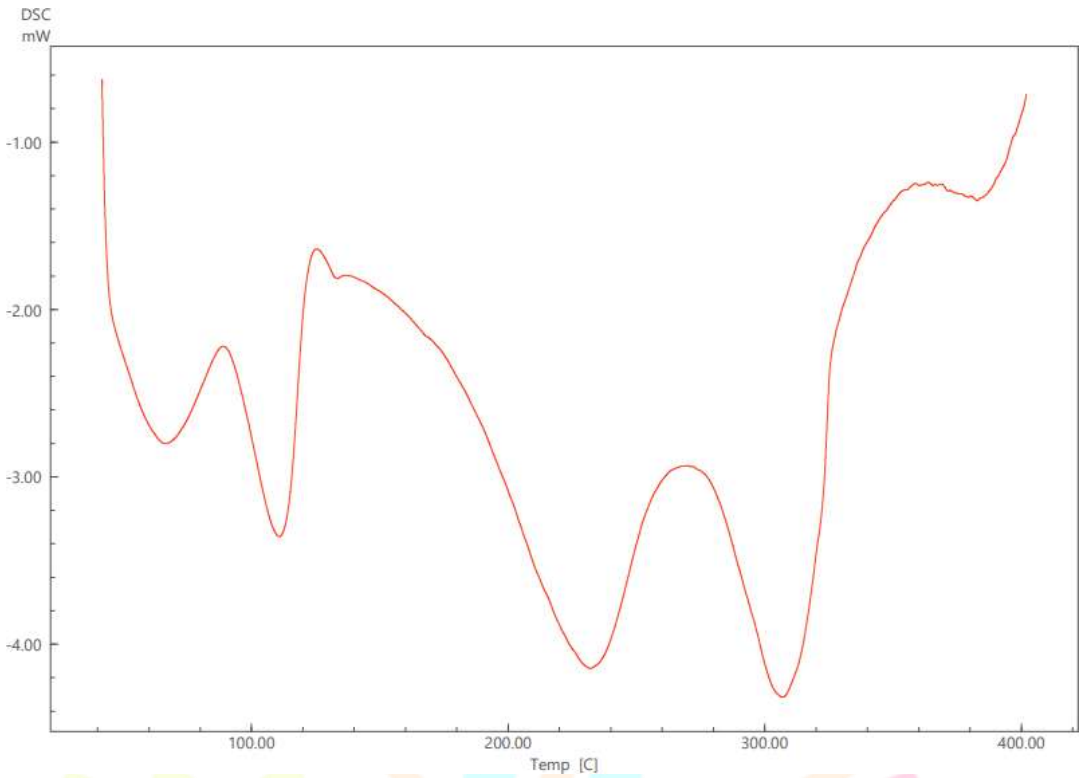

Fig.no.21.Quercetin + Qu-AgNPs (ratio1:1) DSC

The DSC thermogram of quercetin and Carbopol mixture, exhibiting endothermic peak of quercetin 306° C corresponding to its melting and decomposition reported peak temperature 320-325° C.Therefore there is chemical shifting of melting point of quercetin.

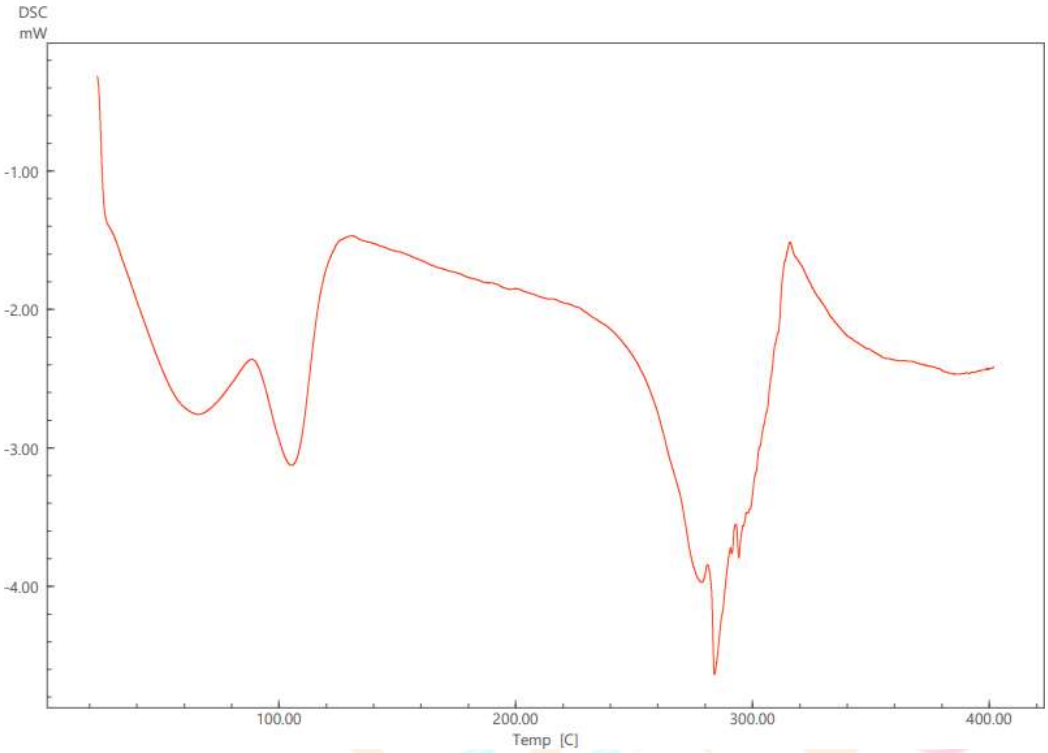

Fig.no.22. Quercetin + extract (ratio1:1) DSC

The DSC thermogram of quercetin and extract , exhibiting an endothermic peak of quercetin 284° C corresponding to its melting and decomposition reported peak temperature 320-325° C. Therefore, there is the chemical shifting the of melting point quercetin.

9. Determination of Quercetin by UV spectroscopy:

UV Spectrophotometer use for Determination of λmax quercetin. UV Analysis is done by using Shimadzu (1900i) double beam UV Spectrophotometer. It shows absorbance maxima (**λmax**) at 373nm in Ethanol. UV spectrum shows peak at 373nm which complies with the USP standard value.

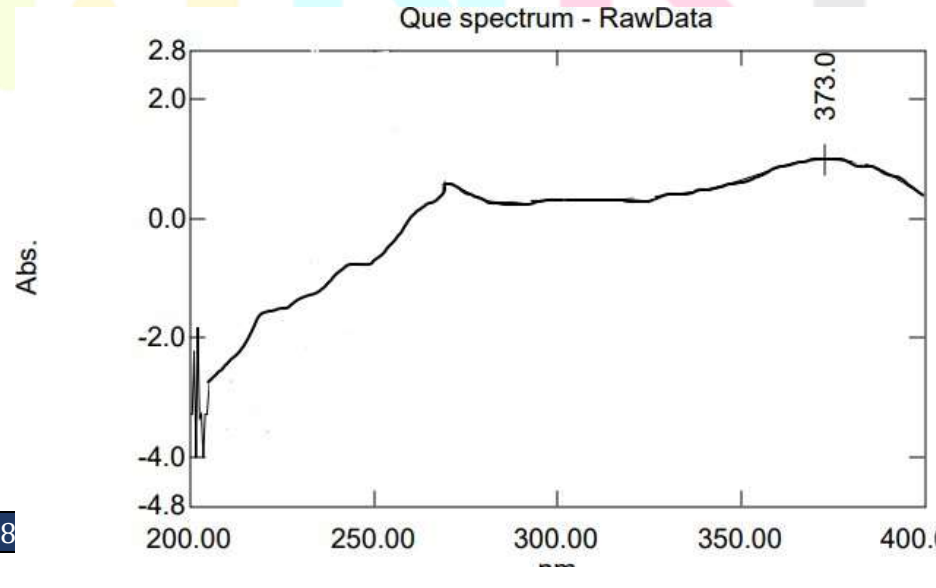

Fig.no.23.UV spectrum of Quercetin.

Calibration curve of quercetin:

The standard calibration curve data for quercetin in ethanol is obtained by plotting the absorbance versus concentration data. The equation of the calibration curve for Quercetin was y=mx+c, where as Linearity was found to be in water is about 0.9797

SrNo	Concentration	Absorbance
1	2	0.159
2	4	0.273
3	6	0.499
4	8	0.647
5	10	0.747
6	12	1.048

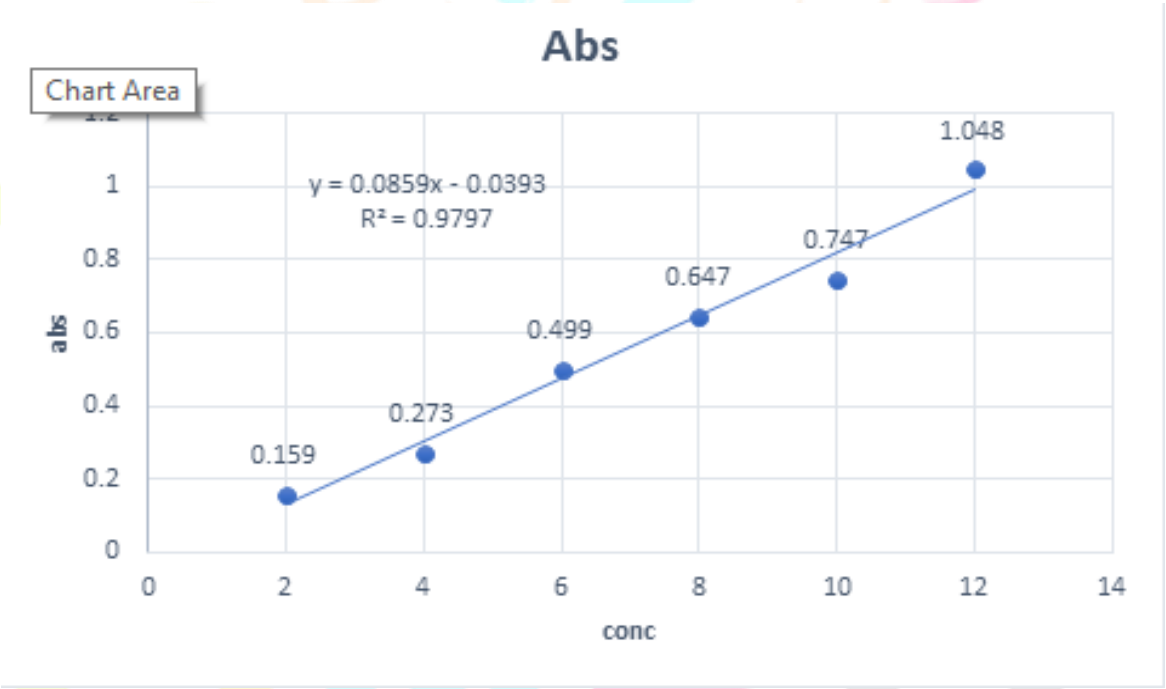

Fig no.24.Quercetin Abs

10. FTIR Spectroscopy:

FTIR is a useful technique used to confirm the formation of an inclusion complex. FTIR Spectroscopy done by using Shimadzu (8400S) by Potassium bromide (KBr) pellet method shows peaks as in following table, that gives conformity of structure of drug.

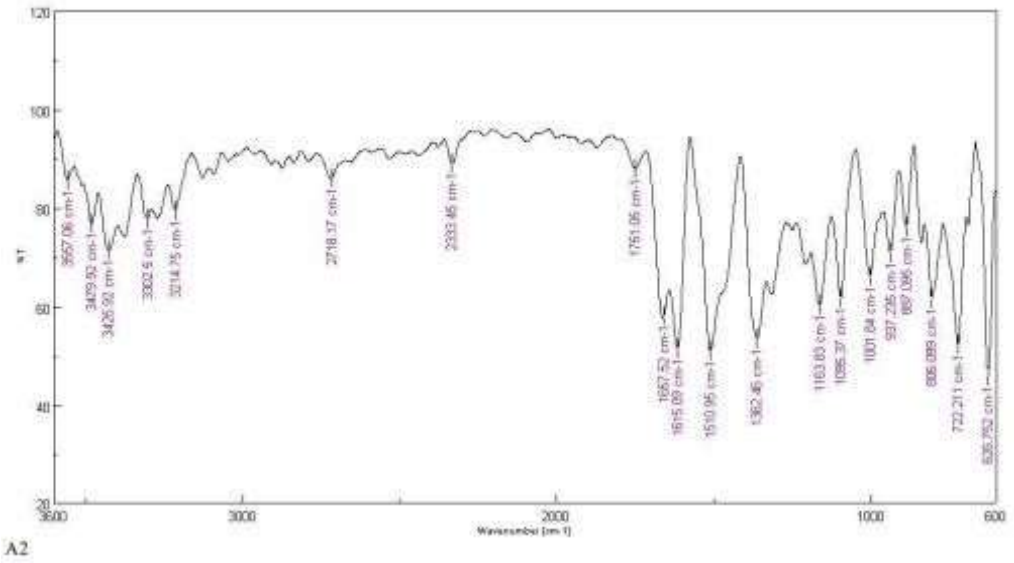

Fig.no.25.FTIR Spectroscopy of Quercetin

Sr.NO	FunctionalGroup	Wavenumber cm^{-1}
1	OH stretching	3214.75
2	C=O carbonyl compound	1751.05
3	C-H bending aromatic	1657.52
4	C=C stretching alkene	1657.52
5	O-H bending phenol	1362.46
6	C-O stretching tart alcohol	1163.83

Table 6. Interpretation of Quercetin

REFERENCE:

1. Alexander JW. History of the Medical Use of Silver. Surg Infect. 2009;10:289–292. doi: 10.1089/sur.2008.9941. [DOI] [PubMed] [Google Scholar]

2. Barillo DJ, Marx DE. Silver in medicine: a brief history BC 335 to present. Burns. 2014;40:S3–S8. doi: 10.1016/j.burns.2014.09.009. [DOI] [PubMed] [Google Scholar]

3. Asgary V, Shoari A, Baghbani-Arani F, Sadat Shandiz SA, Khosravy MS, Janani A. et al. Green synthesis and evaluation of silver nanoparticles as adjuvant in rabies veterinary vaccine. Int J Nanomedicine. 2016;11:3597–3605. doi: 10.2147/IJN.S109098. [DOI] [PMC free article] [PubMed] [Google Scholar]

4. Saratale GD, Saratale RG, Benelli G, Kumar G, Pugazhendhi A, Kim D-S. et al. Anti-diabetic potential of silver nanoparticles synthesized with Argyreia nervosa leaf extract high synergistic antibacterial activity with standard antibiotics against foodborne bacteria. J Clust Sci. 2017;28:1709–1727. [Google Scholar]

5. Shanmuganathan R, Karuppusamy I, Saravanan M, Muthukumar H, Ponnuchamy K, Ramkumar VS. et al. Synthesis of Silver Nanoparticles and their Biomedical Applications - A Comprehensive Review. Curr Pharm Des. 2019;25:2650–2660. doi: 10.2174/1381612825666190708185506. [DOI] [PubMed] [Google Scholar]

6. Stagon SP, Huang H. Syntheses and applications of small metallic nanorods from solution and physical vapor deposition. Nanotechnol Rev. 2013;2:259–267. [Google Scholar]
7. Pourzahedi L, Eckelman MJ. Comparative life cycle assessment of silver nanoparticle synthesis routes. Environ Sci Nano. 2015;2:361–369. [Google Scholar]
8. Iravani S, Korbekandi H, Mirmohammadi SV, Zolfaghari B. Synthesis of silver nanoparticles: chemical, physical and biological methods. Res Pharm Sci. 2014;9:385–406. [PMC free article] [PubMed] [Google Scholar]
9. Dong PV. Chemical synthesis and antibacterial activity of novel-shaped silver nanoparticles. Int Nano Lett. 2012. p:2-9.
10. Zhang Z, Zhang X, Xin Z, Deng M, Wen Y, Song Y. Synthesis of monodisperse silver nanoparticles for ink-jet printed flexible electronics. Nanotechnology. 2011;22:425601. doi: 10.1088/0957-4484/22/42/425601. [DOI] [PubMed] [Google Scholar]
11. Chevallier, Andrew. Encyclopedia of Medicinal Plants. London: Dorling Kindersley, 1996.
12. PDR for Herbal Medicines. Montvale, N. J.: Medical Economics Company, 1999.
13. Peirce, Andrea. The American Pharmaceutical Association Practical Guide to Natural Medicines New York: William Morrow and Company, 1999.
14. Sharifi N, Mahernia S, Amanlou M. Comparison of different methods in quercetin extraction from leaves of Raphanus sativus L. Pharmaceutical Sciences. 2016; 23: 59–65.
15. Chen, J.; Li, S.; Chen, Y.; Yang, J.; Dong, J.; Lu, X. L-Cysteine-Terminated Triangular Silver Nanoplates/MXene Nanosheets Are Used as Electrochemical Biosensors for Efficiently Detecting 5-Hydroxytryptamine. Anal. Chem. 2021, 93, 16655–16663.
16. Ahalwat, S.; Bhatt, D.C.; Rohilla, S.; Jogpal, V.; Sharma, K.; Virmani, T.; Kumar, G.; Alhalmi, A.; Alqahtani, A.S.; Noman, O.M.; et al. Mannose-Functionalized Isoniazid-Loaded Nanostructured Lipid Carriers for Pulmonary Delivery: In Vitro Prospects and In Vivo Therapeutic Efficacy Assessment. Pharmaceuticals 2023, 16, 1108
17. Tasca, F.; Antiochia, R. Biocide Activity of Green Quercetin-Mediated Synthesized Silver Nanoparticles. Nanomaterials 2020, 10, 909.
18. Apriani E F, Miksusanti M, Fransiska N. Formulation and optimization peel off gel mask with polyvinyl alcohol and gelatin basedusing factorial design from banana peel flour (Musa paradisiaca L)as antioxidant.Indonesian Journal of Pharmacy.2022.
19. Singh D, S M Rawat M, Semalty A, Semalty M. Quercetin- phospholipid complex: an amorphous pharmaceutical system in herbal drug delivery. Current Drug Discovery Technologies.2012Mar1; 9(1):17-24.
20. Ice C H, Wender S H. Quercetin and its glycosides in leaves of Vacciniummyrtillus. Journal of the American Chemical Society.1953Jan; 75(1):50-2.
21. Da Costa E M, Barbosa Filho J M, do Nascimento T G, Macêdo R O. Thermal characterization of the quercetin and rutin flavonoids. Thermo chimica Act a. 2002 Sep 15; 392:79-84.
22. Shirazi O U, Khattak M M, Shukri N A, Nasyriq M N. Determination of total phenolic, flavonoid content and free radical scavenging activities of common herbs and spices. Journal of Pharmacognosy and Phytochemistry.2014;3(3):104-8.
23. Patil V, Angadi S, Devdhe S. Determination of quercetin by UV spectroscopy as quality control parameter in herbal plant : Cocculushirsutus. Journal of Chemical and PharmAceutical Research. 2015; 7(1):99-104.
24. Milanezi F G, Meireles L M, de Christo Scherer M M, de Oliveira J P, da Silva A R, de Araujo M L, Endringer D C, Fronza M, Guimarães M C,Scherer R. Antioxidant, antimicrobial and cytotoxic activities of gold nanoparticles capped with quercetin. Saudipharmaceuticaljournal.2019Nov1; 27(7):968-74.

25. Zhang L, Yang X, Li S, Gao W. Preparation, physicochemical characterization and invitro digestibility on solid complex of maize starches with quercetin. LWT-Food ScienceandTechnology.2011Apr1; 44(3):787-92.
26. Chen ZP, Sun J, Chen HX, Xiao YY, Liu D, Chen J, Cai H, Cai BC. Comparative pharmacokinetics and bioavailability studies of quercetin, kaempferol and isorhamnetin after oral administration of Ginkgo biloba extracts, Ginkgo biloba extract phospholipid complexes and Ginkgo biloba extract solid dispersions in rats. Fitoterapia. 2010 Dec1; 81(8):1045-52.
27. Jamadar M J, Shaikh RH. Preparation and evaluation of herbal gel formulation. Journal of Pharmaceutical Research and Education. 2017; 1(2):201-4.
28. Apriani E F, Miksusanti M , Fransiska N. formulation and optimization peel-off gel mask with polyvinyl alcohol and gelatin basedusing factorial design from banana peel flour (musa paradisiaca l) as antioxidant. Indonesian Journal of Pharmacy.2022.
29. M Ana, Pascual-D. Inorganic-Nanoparticle Modified Polymers. Polymers. 2022; 14(10): 1-5.
30. Khan I, Saeed K, Khan I. Nanoparticles: Properties, applications and toxicities. Arabian Journal of Chemistry. 2019; 12(7): 908-931.
31. Alshammari BH, Lashin A MM, Mahmood AM, Al-Mubaddel SF, llyas N, Rahman N, Sohail M, Khan A, Abdullaev SS and Khan R. Organic and inorganic nanomaterials: fabrication, properties and applications.RSC Adv. 2023; 13: 13735–13785.