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Design and Development of Quercetin Loaded Silver Nanoparticles for Antibacterial Activity

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Abstract: ***Nanotechnology has gained huge attention over time. It be spherical, cylindrical, tubular, conical, hollow core, spiral, flat, etc. or irregular and differ from 1 nm to 100 nm in size. . Biodegradable polymeric nanoparticles, particularly those coated with hydrophilic polymer such as poly(ethylene glycol) (PEG) known as long-circulating particles, have been used as potential drug delivery devices because of their ability to circulate for a prolonged period time target a particular organ. Quercetin (Qu) is one of the major bio flavonoid and forms the backbone of many other flavonoids. Materials: Quercetin (Konark Herbal & Health Care Pvt. Ltd., HP), Silver nitrate (Thermo Fisher Scientific Pvt. Ltd., Mumbai), Tri sodium citrate (Nice chemicals Pvt. Ltd., Mumbai, India), Methanol (LOBA CHEMIE Pvt. Ltd., Mumbai). silver nanoparticle containing quercetin is an attempt to utilize the potential of Ag NPs as a carrier to increase the activity of quercetin. So, we developed and evaluate the Ag NPs containing quercetin to obtain the optimized formulation with increased antibacterial activity. Discussion: Formulate and evaluate silver NPs containing quercetin for drug delivery in resistant microbial strains. In-vitro evaluation of silver NP formulation for the release characteristics of drug. Determination of antibacterial activity of silver NP containing quercetin. Conclusion: Quercetin is used in the treatment of infection caused by Escherichia coli, Streptococcus aureus, Pseudomonas aeruginosa, Helibacter pylori, other gram negative and gram positive bacteria. Ag NPs formulation of quercetin alters the chemical structure of quercetin and it becomes active against resistant bacteria. The Ag NPs containing quercetin were prepared by chemical reduction method and evaluated. Based on R^2 value the formulation followed First order model.***

Keywords: Silver nanoparticles, Quercetin, Antibacterial Activity, Trisodium citrate

1. Introduction

Nanotechnology has gained huge attention over time. The nanoparticles are different shape, size and structure. It be spherical, cylindrical, tubular, conical, hollow core, spiral, flat, etc. or irregular and differ from 1 nm to 100 nm in size. Nanocapsules are the systems in which the drug is confined to a cavity surrounded by a unique polymer membrane, while nanospheres are matrix system in which the drug is physically & uniformly dispersed. Biodegradable polymeric nanoparticles, particularly those coated with hydrophilic polymer such as poly(ethylene glycol) (PEG) known as long-circulating particles, have been used as potential drug delivery devices because of their ability to circulate for a prolonged period time target a particular organ, as carriers of DNA in gene therapy, and their ability to deliver proteins, peptides and genes. Silver nanoparticles (Ag NPs) have shown excellent bactericidal properties against a wide range of microorganisms.

Advantages

- Particle size and surface characteristics of NPs can be easily manipulated to achieve both passive and active drug targeting after parenteral administration.
- They control and sustain release of the drug during the transportation and at the site of localization, altering organ distribution of the drug and subsequent clearance of the drug so as to achieve increase in drug therapeutic efficacy and reduction in side effects.
- Controlled release and particle degradation characteristics can be readily modulated by the choice of matrix constituents. Drug loading is relatively high and drugs can be incorporated into the systems without any chemical reaction, this is an important factor for preserving the drug activity.
- The system can be used for various route of administration including oral, nasal, parenteral, intra-ocular etc.

Silver Nanoparticles:

Silver nanoparticles (Ag NPs) have shown excellent bactericidal properties against a wide range of microorganisms. They are prepared from different perspectives, often to study their morphology or physical characteristics. The Ag NPs and their application in electronics, catalysis, Many metal salts and metal nanoparticles have been found to be effective in inhibiting the growth of many infectious bacteria. Silver and Ag NPs occupy a prominent place in the series of such metals which are used as antimicrobial agents from time immemorial. Silver salts are used to inhibit the growth of a variety of bacteria in human system. Small sized Ag NPs are excellent growth inhibitors of certain bacteria.

Nanosilver

Nanosilver (NS), comprising silver nanoparticles is attracting interest for a range of biomedical applications owing to its potent antibacterial activity. Nanosilver has useful anti-inflammatory effects and improves wound healing, which could be used in developing better dressings for wounds and burns. Its broad-acting and potent antibacterial activity is the multifaceted mechanism by nanosilver acts on microbes.

Characterization techniques of nanoparticles

After green synthesis of nanoparticles, characterization is an important step to identify the nanoparticles by their shape, size, surface area and dispersity. To characterize nanomaterials various techniques are employed of AgNPs possesses the following advantages over traditional chemical methods.(i) Green synthesis is simple and usually involves a one-pot reaction; (ii) it is amenable to scale up;(iii) the toxicity associated with hazardous chemicals are eliminated,

(iv) green biological entities can be used as reducing and capping agents, and(v) finally, the process is cost-effective, require little intervention or input of energy, uses renewable resource, environmental friendly method and it is not necessary to use high pressure, energy, temperature and toxic chemicals. The green synthesis of AgNPs involves three main steps based on green chemistry perspectives: (i) selection of a biocompatible and non-toxic solvent medium, (ii) selection of environmentally benign reducing agents, and (iii) selection of non-toxic capping and stabilizing agent for stabilization of AgNPs. The main mechanism considered for the green synthesis of AgNPs process is plant assisted reduction due to phytochemicals present in extracts.

Antibacterial properties of silver nanoparticles

Metal NPs have been the subject of research interest because of their unique properties, such as electronic, optical, mechanical, magnetic and chemical properties are significantly different from the bulk material. The physical and chemical properties of NPs are function of their size/shape and are therefore different as compared to size independent constant physical properties of bulk material. Properties of AgNPs are significantly different from bulk silver metal. The size, shape, and surface morphology of AgNPs play a vital role in controlling their properties. Silver has been extensively used as a therapeutic for several diseases since from ancient times. Before the establishment of antibiotics treatment, silver was used as an antiseptic agent for the treatment of burns and open wounds. The antibacterial activity of AgNPs on gram negative and gram positive bacteria is not similar but competes for one over the other. There are contradictory conclusions regarding the antibacterial activity of AgNPs against gram negative and gram positive bacteria.

Quercetin

Quercetin (Qu) is one of the major bio flavonoid and forms the backbone of many other flavonoids. It is dietary flavonoid, distributed in onion, apple, berries, tea and brassica vegetables, as well as many nuts, seeds, barks, flowers and leaves. Qu also found in medicinal botanicals such as *Solanum trilobatum*, *Ginkgo Biloba* and many others. The predictable daily dietary intake of Qu by a person in United States is 25mg. Qu is a major constituent of various food supplements and other nutraceuticals.

2. Materials and Method

2.1 Materials

Quercetin (Konark Herbal & Health Care Pvt. Ltd., HP), Silver nitrate (Thermo Fisher Scientific Pvt. Ltd., Mumbai), Tri sodium citrate (Nice chemicals Pvt. Ltd., Mumbai, India), Methanol (LOBA CHEMIE Pvt. Ltd., Mumbai, India)

2.2 Method

Method of synthesis of silver nanoparticles Synthesis of silver nanoparticles using trisodium citrate (TSC) as a reducing agent. Silver nitrate and trisodium citrate were used as starting materials for the preparation of silver nanoparticles. The silver colloid was prepared by using chemical reduction method. All solutions of reacting materials were prepared in distilled water. In typical experiment 50 ml of 0.001 M AgNO3 was heated to boil. To this solution 5 ml of 1% trisodium citrate was added drop by drop. During the process, solutions were mixed vigorously and heated until change of colour was evident (pale yellow). Then it was removed from the heating device and stirred until cooled to room temperature. 2 gm of quercetin was dissolved in methanol and added to silvernanoparticles.

Preformulation studies

Preformulation study is the first step in the rational development of dosage forms of a drug substance. It can be defined as an investigation of physical & chemical properties of a drug substance alone & when combined with excipients. The overall objective of preformulation testing is to generate information useful to the formulator in developing stable & bio available dosage forms. Following preformulation studies were performed.

Organoleptic properties

The organoleptic studies like general appearance like colour, nature, odour etc. were performed by visual observations & compared with standard of drug given in pharmacopoeia for the identification of drug.

Colour: Small quantity of drug was taken on butter paper & viewed in well illuminated place.

Odour: Very less quantity of drug was smelled to get the odour.

Solubility studies: Semi quantitative determination of the solubility was made by adding solvent to glass tube containing accurately weighed amount of solute. The system is vigorously shaken and examined visually for any insoluble solute particles. The solubility is expressed in terms of ratio of solute and solvent. The solubility study of quercetin was performed in methanol, ethanol, acetone, hexane, ether, chloroform, propylene glycol, distilled water, 0.1 N HCL, phosphate buffer solution pH 5.5, 6.8, 7.4, separately by keeping the drug containing test tube on vortex mixture.

Determination of melting point: For determination of melting point USP method was followed. Small quantity of drug was placed into a sealed capillary tube. The tube was placed in the melting point apparatus. The temperature in the apparatus was gradually increased & the observation of temperature was noted at which drug started to melt and the temperature when the entire drug gets melted was noted.

Differential scanning calorimetry (DSC): All dynamic DSC studies of pure drug & drug with polymers were carried out in DSC TA 60 Shimadzu thermal analyzer. The instrument was calibrated using high purity indium metal as standard. The scans were taken in nitrogen atmosphere at the heating rate of 10°C/min.

Determination of partition co-efficient: The known quantity of quercetin was added into 20 ml of octanol & it was mixed with 20 ml of phosphate buffer pH 7.4 in a separating funnel. Then two phases were allowed to equilibrate at 37 ° C for 2 hours with intermittent shaking. The concentration of drug in the aqueous phase & organic phase was determined by UV spectroscopic method at λmax 370 nm after necessary dilution.

Determination of drug pH

The pH of quercetin was determined using digital pH meter for freshly prepared 1% solution of Qu in methanol.

Infrared spectroscopic analysis

The fourier infrared spectrums of moisture free samples of quercetin, trisodium citrate, silver nitrate & mixture of quercetin, trisodium citrate, silver nitrate were recorded on IR spectrophotometer. Infrared spectroscopy of different compounds was performed for identification of that particular compound. FTIR spectroscopy was done using KBr pellets. Various peaks in FTIR spectrum were interpreted for identification of different group in the structure of quercetin. FTIR spectroscopy can also be used to investigate & predict any physicochemical interactions between different components. The scanning range varies from 1700-800 cm^{-1} & the resolution was $1cm^{-1}$.

Analysis by UV-Visible spectroscopy

Determination of wavelength maxima of quercetin: The solution was scanned in the range of 200 to 400 nm to fix the maximum wavelength and UV spectrum was obtained. Preparation of standard curve in methanol Standard stock solution of quercetin: Accurately weighed 100 mg of quercetin & was dissolved in 100 ml of methanol, from this stock solution 10 ml was withdrawn and transferred into 100 ml volumetric flask. Volume was made with methanol in order to get standard stock solution containing 100 µg/ml.

Standard graph of quercetin: From this standard stock solution, a series of dilution (2,4,6, 8, 10,12,14,16,18 and 20 µg/ml) were prepared using methanol. The absorbance of these solutions was measured spectrophotometrically against blank of methanol at 363 nm of quercetin.

Method of synthesis of silver nanoparticle

Synthesis of silver nanoparticles using trisodium citrate (TSC) as a reducing agent. Silver nitrate and trisodium citrate were used as starting materials for the preparation of silver nanoparticles. The silver colloid was prepared by using chemical reduction method. All solutions of reacting materials were prepared in distilled water. In typical experiment 50 ml of 0.001 M AgNO3 was heated to boil. To this solution 5 ml of 1% trisodium citrate was added drop by drop. During the process, solutions were mixed vigorously and heated until change of colour was evident (pale yellow). Then it was removed from the heating device and stirred until cooled to room temperature. 2 gm of quercetin was dissolved in methanol and added to silver nanoparticles.

Evaluation of nanoparticles

Drug entrapment efficiency

The total volume of the nanoparticle suspension was measured. 5 ml of this formulation was diluted with distilled water up to 8 ml and centrifuged at 30,000 rpm for 45 min at 4 ° C using a cooling centrifuge. After centrifugation, the supernatant and sediment were recovered, their volume was measured. Then sediment was analysed using n-propanol and filtered through a 0.45 µm nylon disk filter. The concentration of quercetin in the supernatant and sediment was analyzed by UV-spectrocopic method at 363 nm. The percent drug entrapment was calculated using the following equation:

$$\% \text{ Entrapment efficiency: } \frac{\text{Amount of entrapped drug recovered}}{\text{Total amount of drug}} \times 100$$

Nanoparticle shape and surface morphology

Nanoparticles were visualized using transmission electron microscopy (TEM Philips Technai electron microscope, Netherlands). A drop of nanoparticle solution was dried on a microscopic carbon coated grid, to get absorbed and the surplus was removed by filter paper. A drop of 1% aqueous solution of phosphor tungstic acid (PTA) was then added and left in contact with the sample for 5 mins. The excess solution was removed and the sample was dried at room temperature before the vesicles were viewed under TEM operating at an acceleration voltage of 200 KV.

Particle size measurement

The size of nanparticles was determined by dynamic light scattering method (DLS), using a computerized inspection system (Malvern Zetasizer Nano-ZS, Malvern, U.K.) with DTS nano software. For size measurement, nanoparticle solution was diluted with distilled water and put into curvettes of zetasizer. Then the measurements were conducted at 25 ° C. The DLS measurement were performed over alternating increasing and decreasing temperature cycles at each temperature the sample was equilibrated for at least 3 minutes before performing the measurement. The average hydrodynamic diameter of the nanoparticles under consideration corresponds to the Z-average value measured by DLS. Hence, the data was collected for vesicles size and size distribution.

Zeta potential measurement

Zeta potential is a physical property which is given the net surface charge of the nanoparticles, when these particles inside the solution repelling each other's since produced Coulomb explosion between the charges of the nanoparticles giving rise to no tendency for the particles to agglomerate. The criteria of stability of NPs are measured when the values of zeta potential ranged from higher than +30 mV to lower than -30 mV. Surface zeta potentials were measured using the laser zeta meter (Malvern zeta seizer 2000, Malvern). Liquid samples of the nanoparticles (5 ml) were diluted with double distilled water (50 ml) using NaCl as suspending electrolyte solution (2 x 10-2 M NaCl). The pH was then adjusted to the required value. The samples were taken after

30 minutes. After shaking, the equilibrium pH was recorded and the zeta potential of the metallic particles was measured. A zeta potential was used to determine the surface potential of the silver nanoparticles. In each case, an average of three separate measurements was reported. The criteria of stability of NPs are measured when the values of zeta potential ranged from higher than

+30 mV to lower than -30 mV.

X-ray diffraction

Scattering of X-rays by atoms of a crystal produces interferences so that diffraction pattern gives information on the structure of the crystal or identity of a crystalline substance. 1 ml of the silver nanoparticles solution was spread on a glass slide and dried at 40 ^{o} C in an oven. The process was repeated 3-4 times to obtain a thin film. The spectra were recorded in a Phillips Xpert Pro Diffractometer (Cu Kα radiation, λ1= 1.54056; λ2= 1.54439) running at 40 kV and 30 mA. The diffracted intensities were recorded from 35.01 degrees to 79.99 degrees 2θ angles.

In vitro release studies Drug release kinetics

The release kinetic was studied by various kinetic models as zero order plot, first order plot, higuchi plot and korsmeyer-peppas plot. To study the release kinetics of the nanoparticles data obtained from in-vitro drug release studies were plotted in various kinetic models: zero order as cumulative amount of drug releases vs time, first order as long cumulative % of drug remaining vs time, higuchi model as cumulative % of drug released vs square root of time and korsmeyer-peppas model as log cumulative % drug release vs long time. The best fit model was confirmed by the value of correlation coefficient near to 1.

Zero-order model

Drug dissolution from dosage forms that do not disaggregate and release the drug slowly can be represented by the equation:

$$Q0 - Q1 : K0t \quad (1)$$

Rearrangement of equation (1) yields

$$Q1 : Q0 - K0t \quad (2)$$

Where Q1 is the amount of drug dissolved in time t

Q0 is the initial amount of drug in the solution (most times, Q0 : 0) and K0 is the zero order release constant expressed in units of concentration/time. To study the release kinetics, data obtained from *in vitro* drug release studies were plotted as cumulative amount of drug released versus time.

First order model: This model has also been used to describe absorption and/or elimination of some drugs although it is difficult to conceptualize this mechanism on a theoretical basis. The release of the drug which followed first order rate constant expressed by the equation:

Log C : Log C0 – kt/2.303

Where C0 is the initial concentration of drug, k is the first order rate constant, t is the time. The data obtained are plotted as log cumulative percentage of drug remaining vs. time which would yield a straight line with a slope of – K/2.303.

Application: This relationship can be used to describe the drug dissolution in pharmaceutical dosage forms such as those containing water-soluble drugs in porous matrices.

Higuchi model

Graph was plotted between cumulative percentages of drug released vs. square root of time. Where K is the constant reflecting the design variables of the system and t is the time in hours. Hence, drug release rate is proportional to the reciprocal of the square root of time.

Application: This relationship can be used to describe the drug dissolution from several types of modified release pharmaceutical dosage forms, as in the case of some transdermal systems and matrix tablets with water soluble drugs.

Korsmeyer-Peppas model

Korsmeyer *et al*. (1983) derived a simple relationship which described drug release from a polymeric system. To find the mechanism of drug release, first 60% drug release data were fitted in Korsmeyer-Peppas model

$$Mt/M\infty = Kt^{n}$$

Where Mt/ M are a fraction of drug released at time t, k is the release rate constant and n is the release exponent. The n value is used to characterize different release for cylindrical shaped matrices. For the case of cylindrical tablets, 0.45 n corresponds to a Fickian diffusion mechanism, 0.45 < n < 0.89 to non-fickian transport, n : 0.89 to case 2 (relaxation) transport, and n > 0.89 to super case 2 transport. To find out the exponent of n the portion of the release curve, where Mt/ M < 0.6 should only be used. To study the release kinetics, data obtained from *in vitro* drug release studies were plotted as long cumulative percentage drug release versus log time.

Antibacterial activity studies

Antibacterial activity has been assayed against *Escherichia coli* (gram negative bacteria) by agar well diffusion method. Generally, the antibiotics activity of a compound is expressed in terms of its ability to inhibit the growth of bacteria in nutrient broth or agar. The bacterial inhibition can be measured by disc diffusion method. In this method, discs of standard diameter are made in the nutrient agar medium, containing standard bacterial inoculums. The test compounds are introduced into the disc and the diameter of zone of inhibition was measured.

3. Result and Discussion

Organoleptic properties

The following properties of drug were evaluated and results

are obtained as:

Table 5.1: Organoleptic properties of quercetin

Drug	Test	Specification	Observation
Quercetin	Colour	Yellow crystalline powder	Yellow crystalline powder
Quercetin	Odour	Pungent	Pungent

The observations noted were compared to the specifications given in the pharmacopoeia to confirm the identity of the drug & it was found that observation noted complied with specifications.

Solubility studies

Solubility studies are performed to determine the solubility of drug in different solvents. It is highly soluble in ethanol, methanol and dimethyl formamide (DMF).

Melting point

Melting point of quercetin was found to be 323 ◦ C. Melting point was measured three times and mean was noted.

Differential scanning calorimetry

The DSC thermograms showed sharp endothermic peak corresponding to quercetin melting point 323 ◦ C for quercetin. The DSC thermograms quercetin.

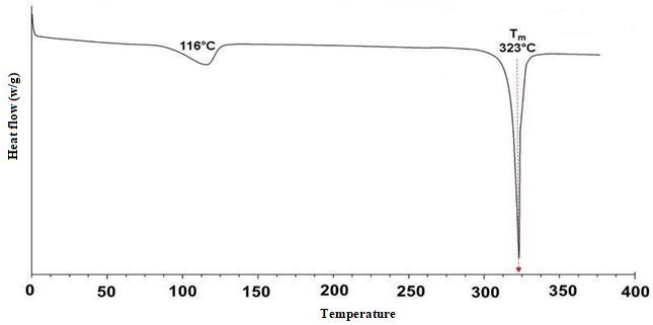


Figure 5.1: DSC thermograms of quercetin

Partition co-efficient

Partition coefficient was measured three times and mean was noted. Hence partition coefficient was found to be 1.82 and the drug is lipophilic.

Determination of pH

The pH was measured three times and mean was noted. Hence pH of quercetin was found to be 2.2.

FTIR analysis

FTIR spectroscopic analysis was carried out to characterize drug. The FTIR spectra obtained was compared with that given in pharmacopoeia for quercetin. Diagnostic peaks and finger print regions were found identical. These characteristics peaks are useful in identification of drug. FTIR of quercetin was done for drug compatibility study.

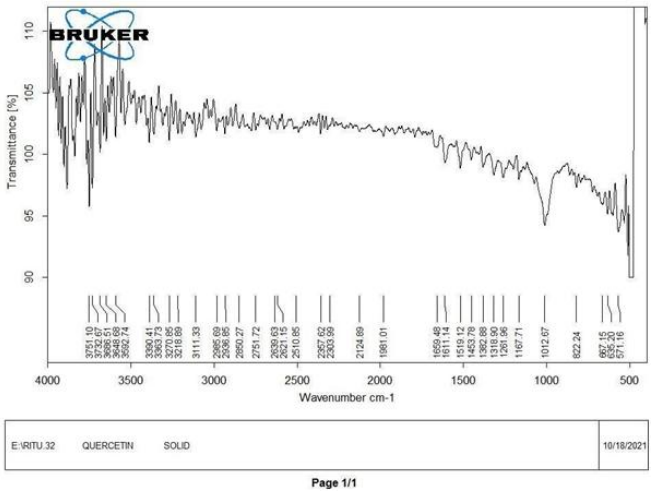


Figure 5.2: FTIR of quercetin

All the groups were present at the same values hence drug sample was genuine and free from any major type of impurities. Analysis by UV-Visible spectrophotometry

Preparation of standard graph:

Stock solution of quercetin: Stock solution of 100 µg/ml was prepared by dissolving 100 mg of quercetin in 100 ml of methanol. Dilution in the range of 10 of 100 µg/ml were scanned for determing max from 200-600 through UV spectrophotometer and λmax was found to be at 363 nm for quercetin.

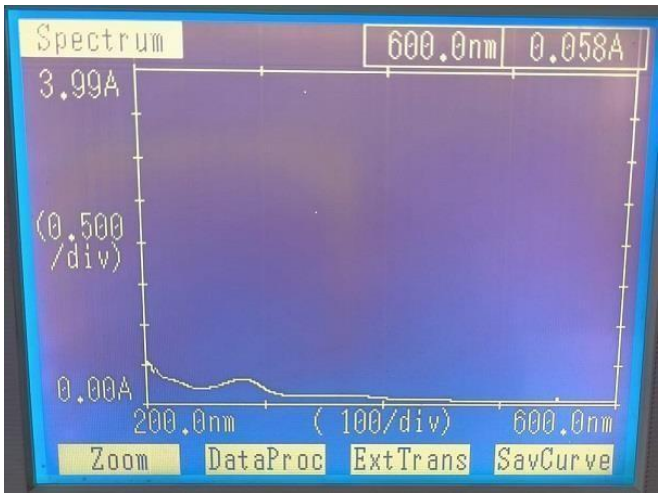


Figure 5.3: UV scan of quercetin in methanol

Preparation of calibration curve in methanol: From this solutions of concentration 2 µg/ml, 4 µg/ml, 6 µg/ml, 8 µg/ml, 10 µg/ml were prepared.

Table 5.2: Absorbance different dilutions of drug at 363 nm in methanol

S.No	Conc. (µg/ml)	Abs.
1.	2	0.005
2.	4	0.022
3.	6	0.032
4.	8	0.035
5.	10	0.040

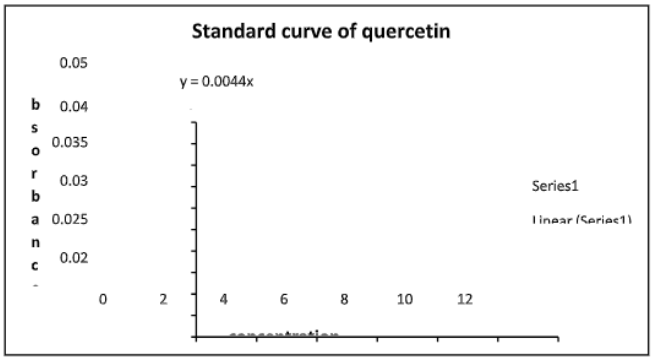


Figure 5.4: Standard calibration curve of quercetin at 363 nm

Evaluation of Nanoparticles

Drug entrapment efficiency

Drug entrapment efficiency was calculated as by formula:

Entrapment efficiency =

Amount of entrapped drug recovered x 100

Total amount of drug

% entrapment efficiency was found to be 65.4%.

Transmission electron microscopy (TEM)

Formulation was selected at best formulation and therefore subjected for TEM to obtain the picture of nanoparticles on scale bar of 200 nm with magnification 13.0 x 4000 as shown below. On characterization spherical, unilamellar vesicles with smooth surface were observed under transmission electron microscopy (TEM).

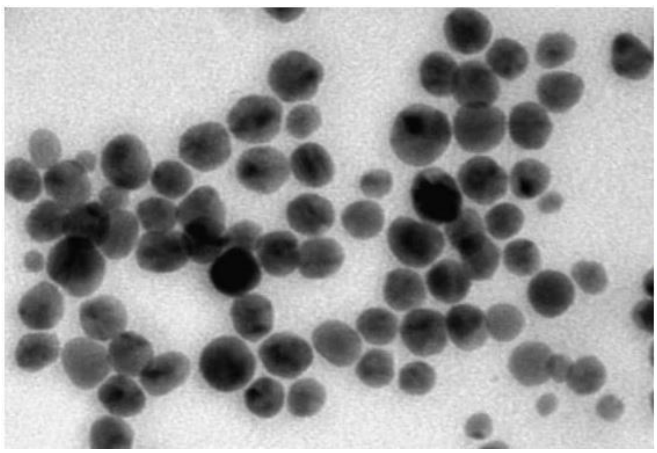


Figure 5.5: TEM of silver nanoparticles

Zeta potential measurement

Zeta potential (mV) : -15.1 + 3.60

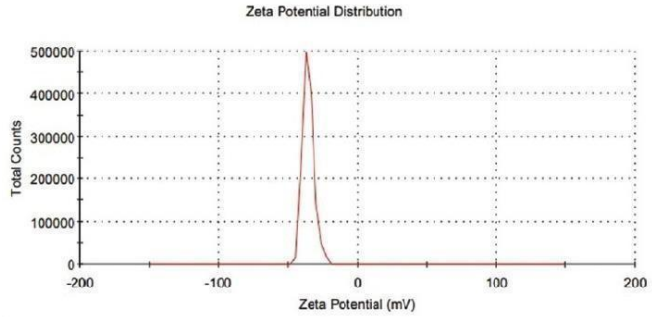


Figure 5.6: Zeta potential

Particle size measurement

Z-Average (d.nm): 129.40 + 0.50 nm

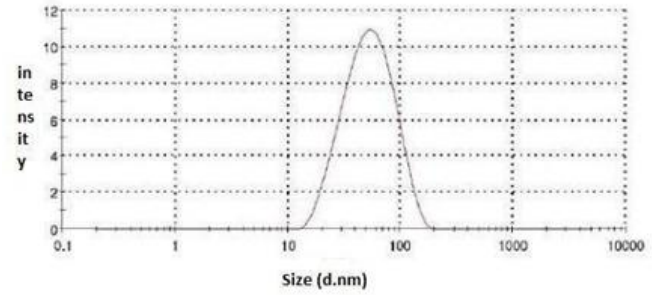


Figure 5.7: Particle size

x-ray diffraction (XRD)

x-ray diffraction pattern reveals that silver nanoparticles exhibit crystalline structure

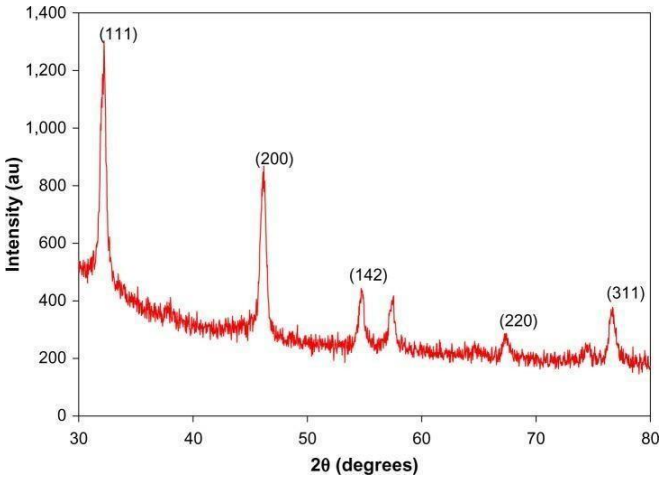


Figure 5.8: X-ray diffraction

***In vitro* release study**

In vitro release study was performed to determine the amount of drug released at different interval of time.

Table 5.3: Release study of quercetin drug

Time (min)	% cumulative release of quercetin drug
0	0
30	5.6
60	10.3
120	19.6
240	35.4

480	54.3
960	75.9
1440	90.6
2880	97.4

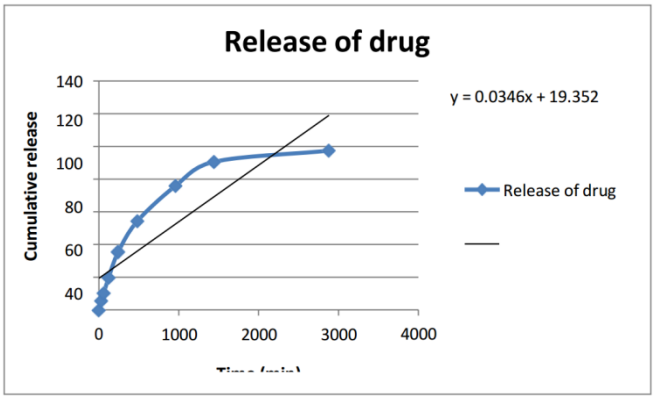


Figure 5.9: Release of drug from formulation in PBS at pH 7.4

Kinetics of drug release

The release kinetic of formulation in PBS of pH 7.4 was studied by various kinetic models. The following data was obtained.

Table 5.4: Drug release data of formulation in PBS at pH 7.4

Time (min)	Log time	Square root of time	% cumulative release of formulation	Log % cumulative release of formulation	% cumulative remaining	Log % cumulative remaining
0	0	0	0	0	100	2
30	1.47	5.47	5.6	0.74	94.4	1.97
60	1.77	7.74	10.3	1.01	89.7	1.95
120	2.07	10.95	19.6	1.29	80.4	1.90
240	2.38	15.49	35.4	1.54	64.6	1.81
480	2.68	21.90	54.3	1.73	45.7	1.65
960	2.98	30.98	75.9	1.88	24.1	1.38
1440	3.15	37.94	90.6	1.95	9.4	0.97
2880	3.45	53.66	97.4	1.98	2.6	0.41

Zero order plot

Graph was plotted between % cumulative drug release vs time

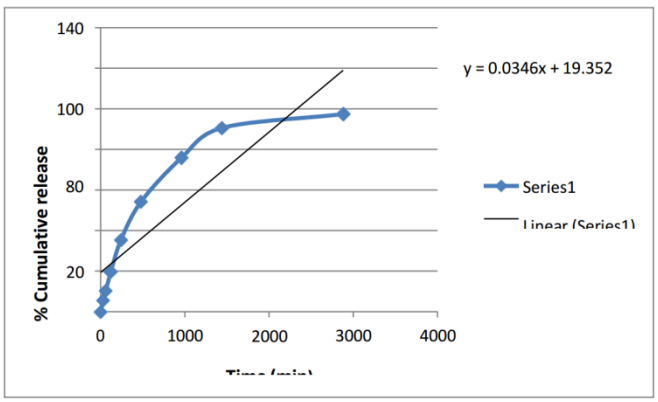


Figure 5.10: Zero order plot for drug release kinetics of formulation First order plot

Graph was plotted between log % cumulative drug remaining vs time

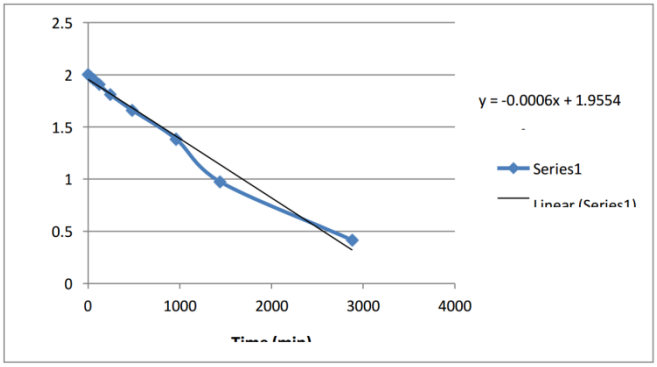


Figure 5.11: First order plot for drug release kinetics of formulation HIGUCHI'S MODEL

Graph was plotted between % cumulative drug release vs square root of time

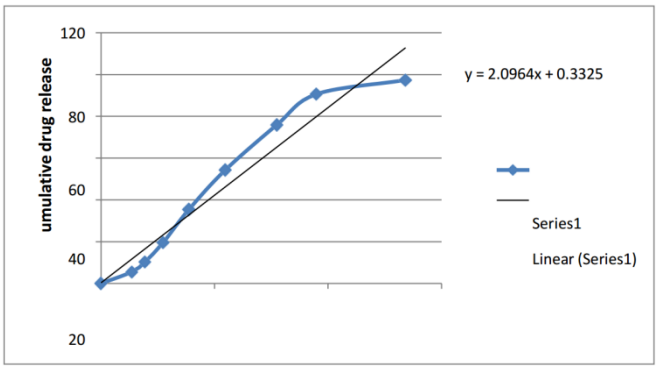


Figure 5.12: Higuchi plot for drug release kinetics of formulation KORSMEYER-PEPPAS MODEL Graph was plotted between log % cumulative drug release vs log time

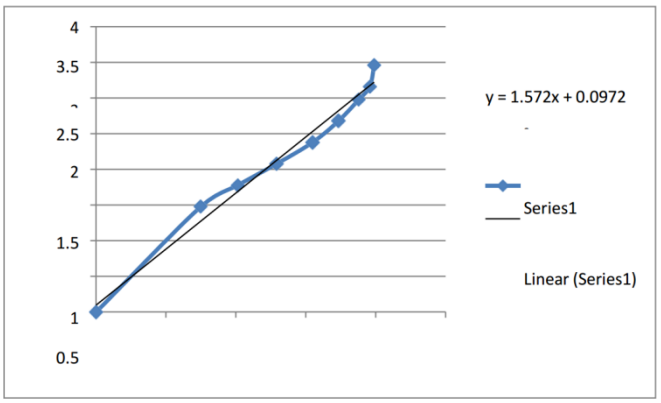


Figure 5.13: Peppas plot for drug release kinetics of formulation

Table 5.5: Kinetics of drug release of formulation

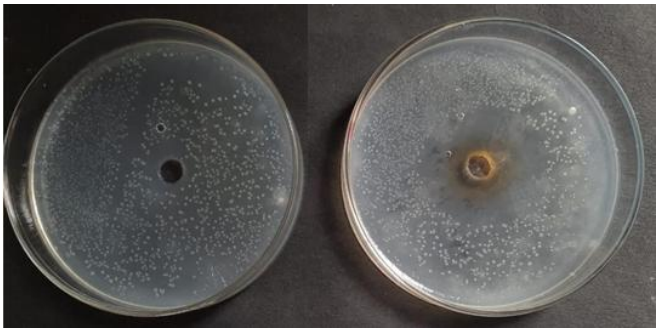
Plot	R^2
Zero order	0.771
First order	0.982
Higuchi model	0.944
Peppas model	0.981

The data obtained for *in vitro* release were fitted into equations for zero order, first order, Higuchi and Korsmeyer Peppas release models. The interpretation of data was based on the value of the resulting regression coefficients. From this values, it was observed that the first order model was

found to be the best suited with R^2 value of 0.982. First order model be used to describe the drug dissolution from several types of modified release pharmaceutical dosage forms.

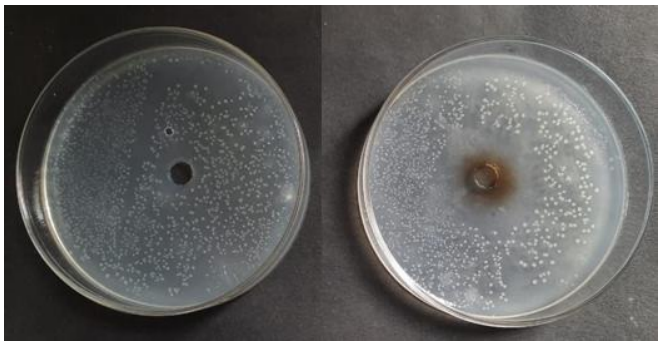
Antibacterial activity

Antibacterial activity was determined by disc diffusion method on *E.coli*.



Control Methanol Quercetin in Methanol

Figure 5.14: Antibacterial activity of quercetin in methanol



Control Water Quercetin in Water

Figure 5.15: Antibacterial activity of quercetin in water

Table 5.6: Antibacterial activity of Ag NPs by disc diffusion method

Result	Zone of inhibition
Control Methanol	0 cm
Quercetin in Methanol	4.4 cm
Control Water	0 cm
Quercetin in Water	4.2 cm

4. Conclusion

The present work on the preparation of silver nanoparticle containing quercetin is an attempt to utilize the potential of Ag NPs as a carrier to increase the activity of quercetin. So, we developed and evaluate the Ag NPs containing quercetin to obtain the optimized formulation with increased antibacterial activity. Quercetin is used in the treatment of infection caused by *Escherichia coli*, *Streptococcus aureus*, *Pseudomonas aeruginosa*, *Helibacter pylori*, other gram negative and gram positive bacteria. Ag NPs formulation of quercetin alter the chemical structure of quercetin and it becomes active against resistant bacteria. The Ag NPs containing quercetin were prepared by chemical reduction method and evaluated. Based on R^2 value the formulation followed First order model.

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