RESEARCH PAPER

Development and *In-vitro* Characterization of Zaltoprofen Loaded SilverNanoparticle Containing Gel forTreatment of Painof Rheumatoid Arthritis

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ABSTRACT

The chronic inflammatory condition known as rheumatoid arthritis is characterized by joint swelling,stiffness,anddestructiontothesurroundingcartilageand bone.Itisanautoimmune disease that is impacted by things like obesity and smoking. By generating interleukin and, cytokines play a crucial role in the degradation of the synovium and cartilage in the joints. Skeletal muscle abnormalities are common in patients with rheumatoid arthritis.

The causes, “pathology”, “development”, “symptoms”, clinical consequences, “diagnosis”, “treatment” choices, medicines, and current patents and applications are all covered in detail in this study on rheumatoid arthritis.

The innovative approaches to treating rheumatoid arthritis and associated conditions are the main focus of the patents. Interleukins, sialoprotein I, tumor necrosis factor-alpha, and other variables are treatment targets. Different forms of rheumatoid arthritis, each having unique pathways, are identified using a variety of biomarkers.A number of commercially available formulations are also listed in the evaluation. The article's primary focus is on current developments in the treatment of rheumatoid arthritis.

Keywords:Rheumatoidarthritis,TNF-α,IL,inflammation,synovium.

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INTRODUCTION

1.1 RheumatoidArthritis

Globally, about 5 out of 1000 persons have rheumatoid arthritis (RA), which can seriously deteriorate joints and cause disability. It often affects women more than men and can appear at any age [1]. Over thepast20years,therehasbeenasubstantialadvancementinourunderstandingofthepathophysiology of RA, the best outcome metrics, and successful therapeutic techniques—such as recognizing the significanceofearlydiagnosisandRAtreatment.Asidefromadvancesinmedicine,thereisnoknown cure for this ailment, and its exact cause is unknown.There aren't many hospitals that offer rheumatic clinical settings run by licensed rheumatologists. There are no national databases to keep track of the different roles that autoimmune illnesses play and the results of their therapies [2, 3].

RAcauses joint damage and disability, increases mortality, and lowers "health-related quality of life." RAisreallyburdensome. Accordingtoestimations,arthritisisoneofthemostexpensivediseases because indirect expenditures, which are based on productivity and disability at work, are four times higher than direct medical expenses.Arthritis-related medical costs and lost productivity cost the US economyapproximately303.5billiondollarsannually[4-6].RApresentsasarticulardegenerationand comorbidities that can interfere with a number of body systems, including bone function, metabolism, and psychological activities. RAaffects 1% of the global population. RAmay be associated with both environmental and genetic risk factors.The "shared epitope" of the MHC class II HLADR allele is a major genetic factor associated with the beginning of RA. Anti-citrullinated antibodies (ACPA) and rheumatoidfactorareexamplesofauto-antibodiesthattypicallyhaveseriousconsequences [7].Early-stage autoimmune dysfunction is thought to be the primary culprit. Cytokines and autoantibodies are examples of systemic immune mediators that are present early in RAand are crucial to the onset and course of

symptoms. This typically develops into established RA, which is characterized by ongoing inflammation that harms nearby tissues and results in abnormalities in joints. Recent developments in immune-targeted treatments, like “kinase inhibitors” and “biologics”, have significantly enhanced clinical care. Cellular and molecular research has also revealed intricate inflammatory processes that contributetothe onset andprogression of RA[8]. Early RAdiagnosis can enhance therapyresultsand prevent joint degeneration. In order to minimize joint loss and improve quality of life, early detection andthebestpossiblecarearecrucialbecausethefirsttwoyearsarecrucialandcanresultinirreversible joint damage. Robust biomarkers are required to provide precise prognosis, prompt diagnosis, and improvedRAtreatment[9].Thegoalofthisprojectistogiveresearchers,physicians,pharmacists,and students up-to-date information about RA.

1.2 Silvernanoparticles

Nanoscale (1–100 nm) materials have properties that are very different from those of their bulk counterparts due to variations inthesurface-to-volumeratioand physicochemicalpropertiesofatoms, molecules, and bulk matter,[14]. Numerous nanomaterials with distinctive properties have been produced as a result of advancements in nanotechnology, opening up a wide range of applications and research possibilities [15]. Silver was utilized to preserve food by ancient societies such the Greeks, Romans,Persians,andEgyptiansapproximately5000yearsago[16].Duetoitsantimicrobialqualities, silverwarewascommonlyusedinantiquityforeating,drinking,andstoringfood[17].Silver hasbeen used medicinally since 300 BC, according to historical documents. Silver utensils are still valued in Hinduismformaking"panchamrit,"aconcoctionofcurdandOcimumsanctum.Thecurativequalities ofspecificmetalsarealsomentionedintheancientAyurvedicliterature"CharakSamhita"[18].Silver wasfrequentlyusedasanantibacterialagentpriorto AlexanderFleming'sdiscoveryofantibiotics.Due to their potent antibacterial properties and the emergence of antibiotic resistance, silver nanoparticles (AgNPs) have recentlyattracted a lot of attention[15].AgNPs' unique qualitiesmakethem useful ina number offields, such as “biomedicine”[19],“medication delivery”[20],“water”“purification” [21], and “agriculture” [22].

Few reviews have addressed the “green synthesis ofAgNPs” in the last ten years; these have largely includedsynthesisfrommicrobialandplantsources,characterisationmethods,sizeandshapedata,and a range of applications [23]–[27].

2. MATERIALS

2.1 Material

Table2.1: ListofChemicals

S.No.	Material	Source
1.	Zaltoprofen	BLDPHARM
2.	Chitosan	Himedia
3.	Silvernitrate	Thomas baker
4.	Carbopol940	BoInternational
5.	Glycerine	Finar
6.	Propyleneglycol	Finar
7.	Potassiumdihydrogenorthophosphate	Finar
8.	SodiumHydroxide	Finar
9.	Tween80	Finar

Table2.2: ListsofInstrumentsused

S.No.	Equipment	Manufacturer
1.	Electronicweighingbalance	Centurion Scientific
2.	pH meter	Electrolab.,Mumbai,India
3.	UVspectrophotometer	Shimadzu
4.	Particlesizeanalyzer	Malvern, UK

3. RESULTANDDISCUSSION

3.1 Preformulationstudies

7.1.1Organoleptic properties

According to the investigation's findings, zaltoprofen is a off white powder with odorless and tasteless.

3.1.2Melting point

A “melting point equipment” and the “capillary” tube method were used to find the melting pointofzaltoprofen.Theinvestigation'sfindingsconfirmedthatthemeltingpointof

zaltoprofen was between 128.33°C±0.58 and 130.00°C±1.00,close to 129–131°C described in the literature [28].

3.1.3.UVspectroscopyofthe zaltoprofen

The "UV-Vis spectrophotometer" was employed to investigate the zaltoprofen working solution absorption maximum.After scanning a 40µg/ml solution of zaltoprofen in methanol diluentinthe"200–400"nmregion,theUVspectrumwasobtained.Thezaltoprofenabsorption maxima, as depicted in Figure 7.1, was confirmed to be 337 nm by the UV spectrum measurement [29].

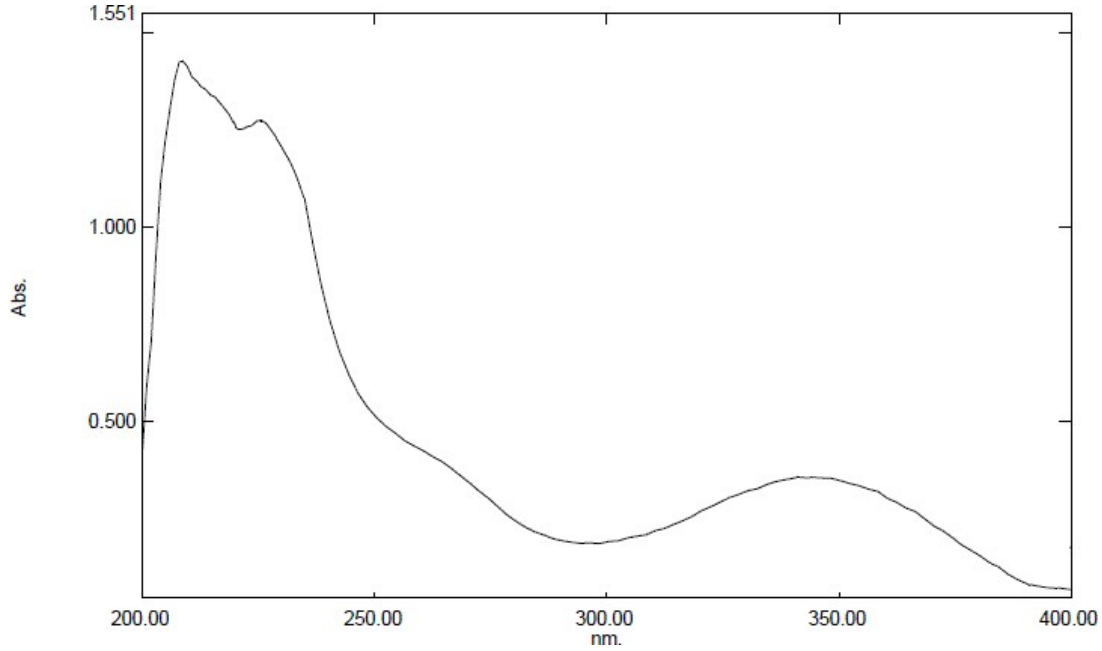


Figure3.1:UVspectrumof40µg/mlconcentrationsolutionof zaltoprofen

3.1.4 StandardlinearitycurveofzaltoprofeninMethanol

TheUVspectrophotometerwasusedtopreparedastandardcalibrationcurveofzaltoprofenin a series of concentration between 10µg/ml to 90µg/ml at 337nm.

Table3.1: Standardlinearitycurveofzaltoprofeninmethanol

S.No.	Concentration(µg/ml)	Absorbance
1	10	0.103±0.002
2	20	0.207±0.005
3	30	0.303±0.003

4	40	0.413±0.004
5	50	0.518±0.003
6	60	0.617±0.005
7	70	0.715±0.005
8	80	0.821±0.003
9	90	0.916±0.005

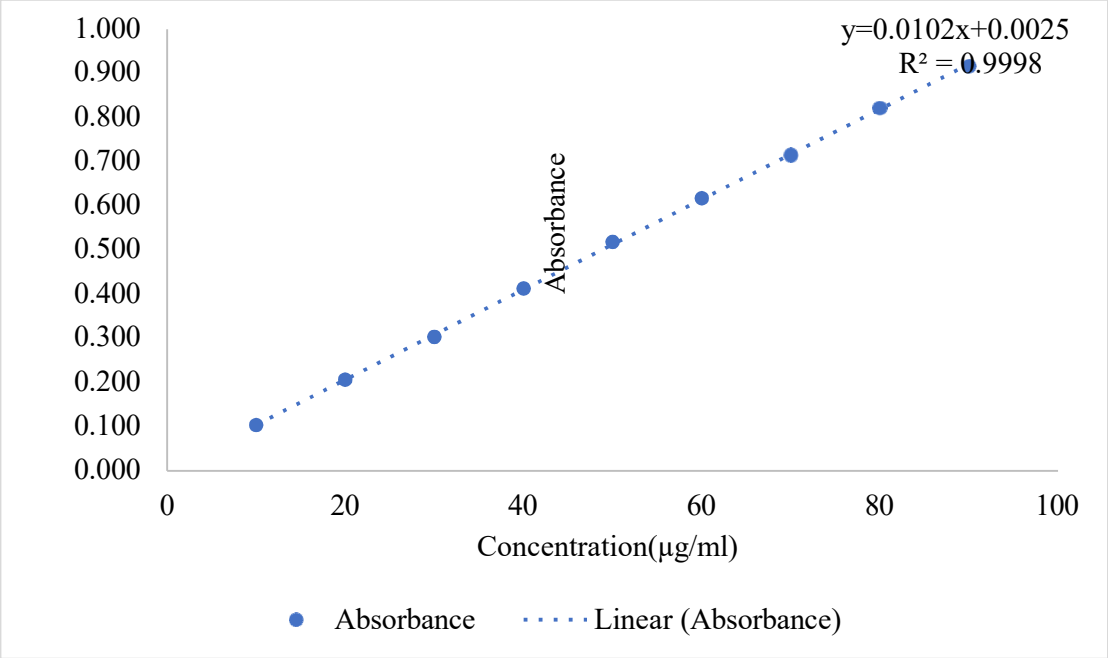


Figure3.2: Lineargraph ofStandardCalibration curveofzaltoprofeninmethanol

Thelinearequationwasdeterminedbyplottingagraphbetweentheabsorbancevaluesattheir respective concentrations of zaltoprofen are shown in Table 3.1. The regression equation for thezaltoprofencalibrationcurveisy=0.0102x+0.0025.Theregressioncoefficientwasfound to be 0.999, demonstrating the equation's linearity.

3.1.5 Solubilitystudiesofdrug

Table 3.2 showed the solubility of the drug moiety in various aqueous and non-aqueous solvents. The findings of the solubility experiment shown in Figure 3.3 [30] show that zaltoprofen drugs are almost insoluble in water and most soluble in methanol and ethanol.

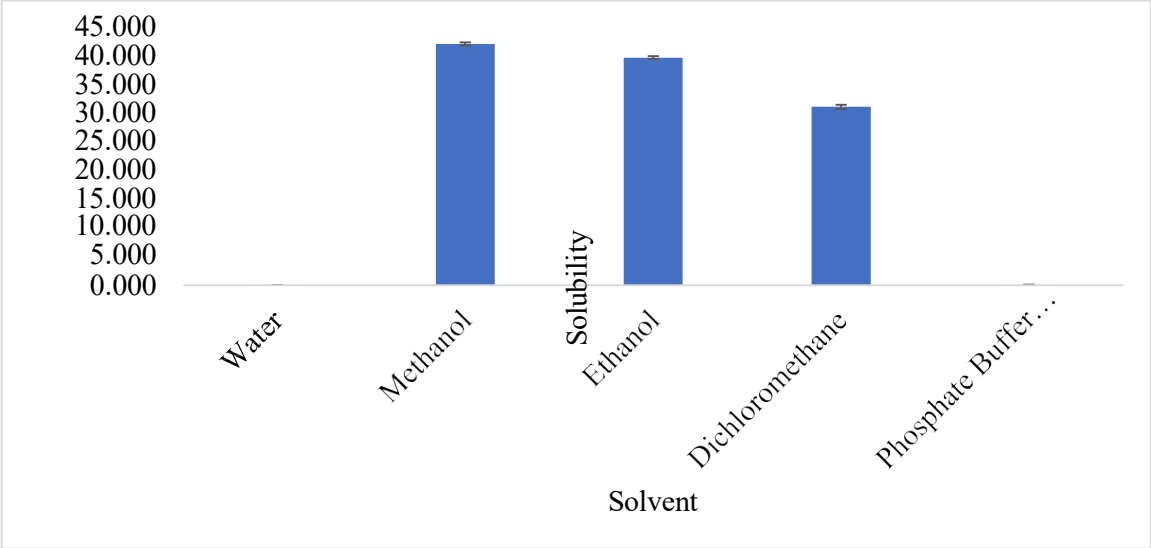


Table3.2: ObservationofSolubilityofinvestigateddruginsolventand buffers

S.No.	Solvent Name	Solubility(mg/ml)	Inference
1	Water	0.084±0.002	Partially insoluble
2	Methanol	42.514±0.255	Soluble
3	Ethanol	40.097±0.268	Soluble
4	Dichloromethane	31.431±0.376	SparinglySoluble
5	PhosphateBuffer6.8pH	0.101±0.003	Partially insoluble

Figure3.3: Observation ofthesolubilityofzaltoprofenin solvent

3.1.6 Partitioncoefficientofthedrug

The results of the current investigation confirmed that zaltoprofen had a partition coefficient of 2.525±0.013, very similar to the 2.57 value indicated in the literature. The findings confirmed that zaltoprofen is a lipophilic drug [31].

3.2 Preparationofsilver nanoparticles

Thechoiceofreducingagentsandtheparticularreactionconditionsusedduringtheirsynthesis have a significant impact on the production of nanoparticles. In this work, silver nitrate was successfullyreducedtothenanoscaleusingsodiumhydroxideandchitosanasreducingagents [32].The firstindication thatnanoparticle formationisbeginningisanoticeable color shiftin thereactionmixture,fromyellowtoyellow-brown.Thelargefreehydroxylandaminogroups in chitosan can convert silver metal to metal nanoparticles. Silver nanoparticles are created when various reducing agents and functional groups chemically convert silver ions (Ag^{+}) to metallicsilver.Typically,thesenanoparticlesaresynthesizedatthreedifferentlevels.Thesilver ionsareextractedfromthesilversulfatesaltbychitosan'sreduction-capablefreehydroxyland aminogroups.Whenreducedsilverionstransformintozero-valentsilveratoms,nucleation occurs.Duringthedevelopmentstage,synthesizedsilvernanoparticlesbuildupandmayvary morphologically [33–35].The final size and shape of the NPs are determined by a number of factors, including the amount of chitosan.

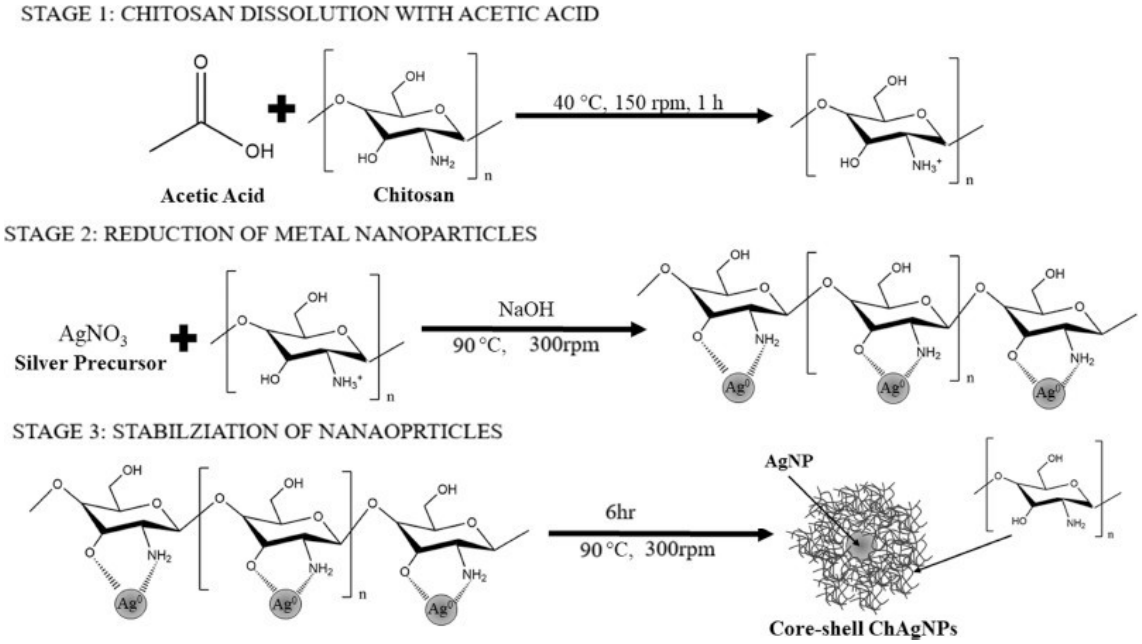


Figure3.4: StepsofChitosandrivensynthesisof Silver Nanoparticles

Figure 3.4 shows the potential mechanism for the creation of nanoparticles, which involves both reduction and stabilization activities mediated by the chitosan solution.Ag + ions were converted toAg0 using chitosan. Free electrons that are generated when alcohol or glucoside groups inside the chitosan molecule oxidize are thought to be the cause of this action. The synthesis of ChAgNPs was also completed in 6 hours due to the higher temperature of 90°C, which accelerates the reduction reaction.An alternative explanation for the reduction process is provided by the amine groups in chitosan, which help transform silver ions into silver nanoparticles. Amines are a commonly used family of organic compounds because they are present in several biological and environmental systems and activities. It has been demonstrated that polysaccharides containing amines, such as chitosan, can serve as dual reductantsandcappingagents.DuringthecreationofChAgNPs,positivelychargedsilverions can be reduced to metallic silver thanks to the primary amine group and its nearby hydroxyl group in the chitosan structure. Furthermore, by creating a matrix around the metal nanoparticles,polymeric aminesfunctionasgrowthregulators,restrictingtheirexpansionand

avoiding agglomeration. AgNPs attain a regulated and consistent size by combining with chitosan to cap the nanoparticles [91].

3.3 Invitrocharacterizationofsilver nanoparticles

3.3.1 Physical appearance

Thephysicalstateofthe synthesizedbatchesofsilvernanoparticlewasshowninTable 3.3.

Table3.3: Physicalappearanceoftheallpreparedbatchesofsilvernanoparticle

S.No.	Formulationcode	Appearance
1	SN1	Browncoloursolutionwithclumpformationbutviscous solution
2	SN2	Browncoloursolutionwithclumpformationbutviscous solution

3	SN3	Browncoloursolutionwithnoclump formation
4	SN4	Yellowcoloursolutionwithnoclumpformation
5	SN5	Yellowcoloursolutionwithnoclumpformation

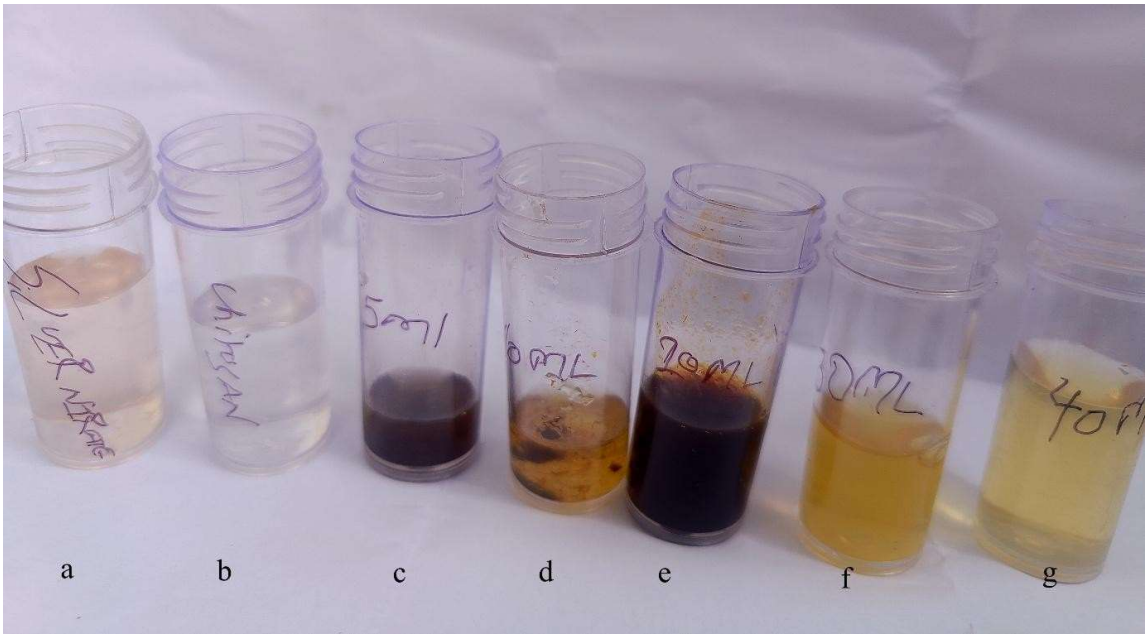


Figure 3.5: Images of prepared batches of the silver nanoparticle a) silver nitrate solution b) chitosan solution, c) silver nanoparticle suspension using 5ml of chitosan solution, d) silver nanoparticle suspension using 10ml of chitosan solution, e) silver nanoparticle suspension using 20ml of chitosan solution, f) silver nanoparticle suspension using 30ml of chitosan solution, g) silver nanoparticle suspension using 40ml of chitosan solution

Incurrentsynthesisofsilvernanoparticles5mL,10mL,20mL,30mL,and40mLofchitosan solutionwasused.Aftershakingduringincubation,theresultantmixtureremainedcompletely soluble with no discernible solid clumps, and just a little amount of chitosan solution was needed.Thecolorshiftfromyellowtoyellowbrownindicatedthesyntehsisof ChAgNPs.Such an observation indicates the formation of silver nanoparticles.According to theTable 3.3, the formulation madewith alittleamountofchitosan(5ml and 10ml)produced abrown color, a viscous solution, and a clump. The formulation SN3 had a darker, more intense brown color. Thelattertwo formulations,SN4andSN5,showedupasyellowsolutions."Surfaceplasmon resonance", an optical phenomenon, which is accountable for the color change in the suspension of silver nanoparticles during synthesis. It is commonly used to monitor how an analyte interacts with a surface-fixed biomolecule. The formation of the nanoparticles is indicatedbythephenomenawherethesolutioncolorturnfrom,yellowtobrown.Ag^{+}reduction was shown by the colorless chitosan solution turning light yellow and eventually yellowish brown. Agglomeration into oligomeric clusters is said to follow the reduction ofAg^{+} by the reducingagent,whichalsoresultsinmetallicsilverproduction.Theseclustersultimatelylead to the formation of "metallic colloidal silver nanoparticles". In current investigation, the biopolymer employed as a protective agent and keep nanoparticle away from aggregating or losingtheirdistinctivecharacteristics.Theoutcomesreportedby otherresearchers[91,35]are consistent with the results achieved here.

3.3.2 Percentagerecovery

Table 3.4 displayed the percentage recovery of the silver nanoparticle batches that were manufactured.Itwasfoundthatthemanufacturedbatchesofsilvernanoparticleshadrecovery percentagesrangingfrom35.033±0.141%to45.119±0.092%.Amaximumpercentageyieldof 45.119±0.092% was shown for formulation SN3. Since SN1 and SN2 formulations were viscous solutions rather than powders, they were excluded.

Table3.4: Percentagerecoveryofthepreparedchitosan-silvernanoparticles

S.No.	Batchcode	Percentagerecovery(%)
1	SN3	45.119±0.092
2	SN4	35.033±0.141
3	SN5	36.888±0.905

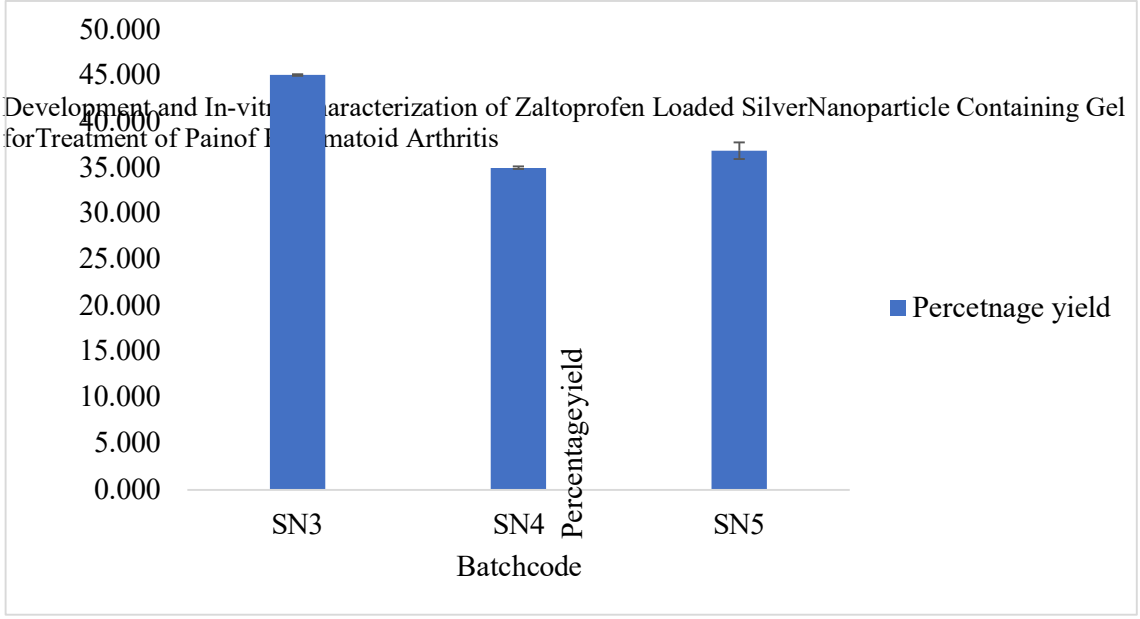
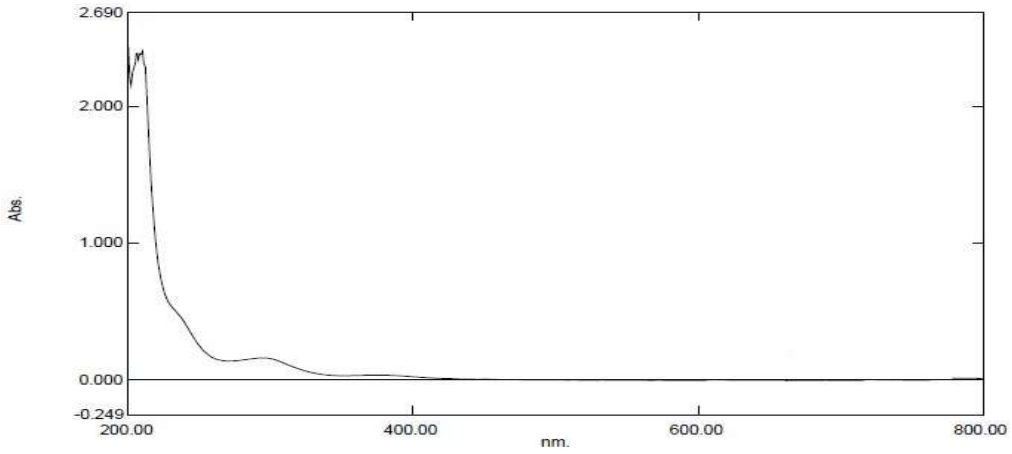


Figure3.6: Percentagerecoveryofthepreparedchitosan-silvernanoparticles
On the basis of these observations, the formulation SN3 was selected for the loading of the zaltoprofen drug.

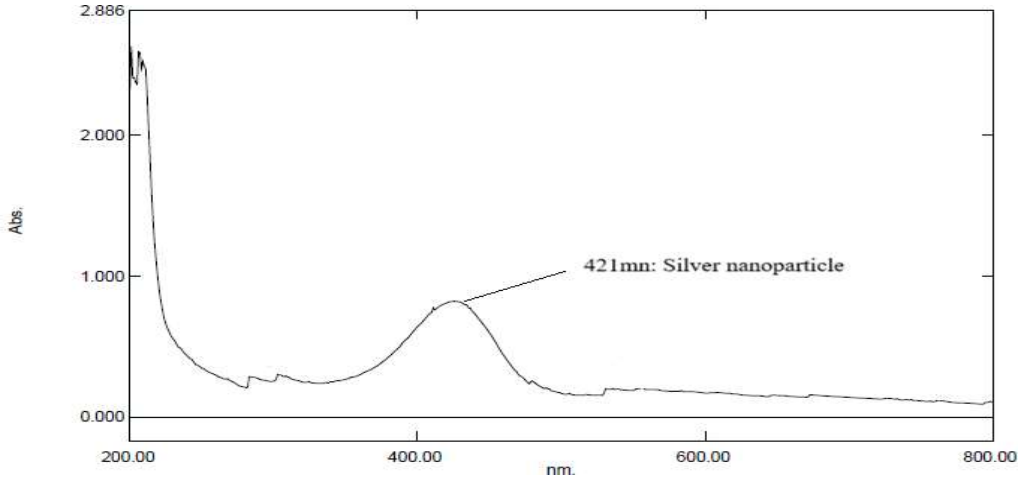
3.3.3 *UVanalysisof sample*

TheanalysisofthechitosansampleandpreparedbatchSN3wasanalyzedfortheconfirmation of the preparation of the silver nanoparticle using the UV spectroscopy as demonstrated in Figure 3.7-3.8.



No.	P/V	Wavelength	Abs.	Description
1	↑	765.00	0.016	
2	↑	718.00	0.002	
3	↑	663.00	-0.002	
4	↑	377.00	0.035	
5	↑	295.00	0.162	
6	↑	206.00	2.419	
7	↓	354.00	0.030	
8	↓	272.00	0.137	

Figure3.7:UVspectrumofthechitosansolution



No.	P/V	Wavelength	Abs.	Description
1	↑	764.00	0.118	
2	↑	727.00	0.136	
3	↑	421.00	0.821	
4	↓	759.00	0.108	
5	↓	508.00	0.146	
6	↓	306.00	0.229	

Figure3.8:UVspectrumofthepreparedsilvernanoparticle formulationSN3

Silvernanoparticlesexhibitaprominentsurfaceplasmonresonance(SPR)peak,whichmakes theUV–visibleabsorptionspectraextremelysensitivetotheirproduction.Theoverlayspectra of the SN3 silver nanoparticle solution and the chitosan solution are displayed in Figures 3.7 and 3.8. When AgNO3 surface plasmon resonance (SPR) was excited, the Chi-Ag-NPs composite displayed an SPR peak at 421 nm. This distinctive band at 421 nm shows how the amino and hydroxyl groups of the chitosan polymer interact with silver ions. The chitosan solution showed no peak becauseAg-NPs were absent (Figure 3.7) [97, 36].

Basedontheaforementionedfindings,thezaltoprofenmedicationwasloadedintoformulation SN3.

3.4 Preparationofthezaltoprofenloadedsilver nanoparticles

Zaltoprofen was added to the silver nanoparticle formulation for this activity at four concentrations:1,2,3,and4mg/mL.Theessentialcharacterisationpropertiesoftheresultant drug-loaded silver nanoparticles were assessed.

3.5 Invitroofthezaltoprofenloadedsilver nanoparticles

7.5.1Physicalappearance

Table 3.5 displayed the synthesized zaltoprofen-loaded silver nanoparticles' physical characteristics.Themanufacturedbatchesofzaltoprofen-loadedsilvernanoparticlesappeared as a dark yellow-brown suspension, according to the observation.

Table3.5: Physicalappearanceofpreparedzaltoprofenloadedsilvernanoparticle

S.No.	Formulationcode	Physicalappearance
1	SN3Z1	Darkyellow-browncolor suspension
2	SN3Z2	Darkyellow-browncolor suspension
3	SN3Z3	Darkyellow-browncolor suspension
4	SN3Z4	Darkyellow-browncolor suspension

3.5.2 Percentagedrugentrapmentandpercentagedrugloading

Table 3.6 displayed the %drugloading and entrapment ofthe synthesized zaltoprofen-loaded silver nanoparticle [94]. High loading capacity and structural stability are essential for drug carriers. Determining the maximum drug-loading capacity and the related conditions is therefore crucial. According to the observation, the generated zaltoprofen-loaded silver nanoparticle's percentage drug loading and entrapment ranged from 8.248±0.209% to 45.466±0.490% and 32.990±0.828% to 60.621±0.654%, respectively. Formulation SN3Z3 producedthehighestpercentageofdrugentrapmentanddrugloadingamongallmanufactured formulations (60.621±0.654% and 45.466±0.490, respectively), demonstrating the silver nanoparticle's appropriateness for the medication zaltoprofen [94].

Table3.6:%drugentrapmentofpreparedbatchesofzaltoprofenloadedsilver nanoparticle

S.No.	Formulationcode	Percentagedrugentrapment(%)
1	SN3Z1	32.990±0.828
2	SN3Z2	49.265±0.490
3	SN3Z3	60.621±0.654
4	SN3Z4	42.443±0.510

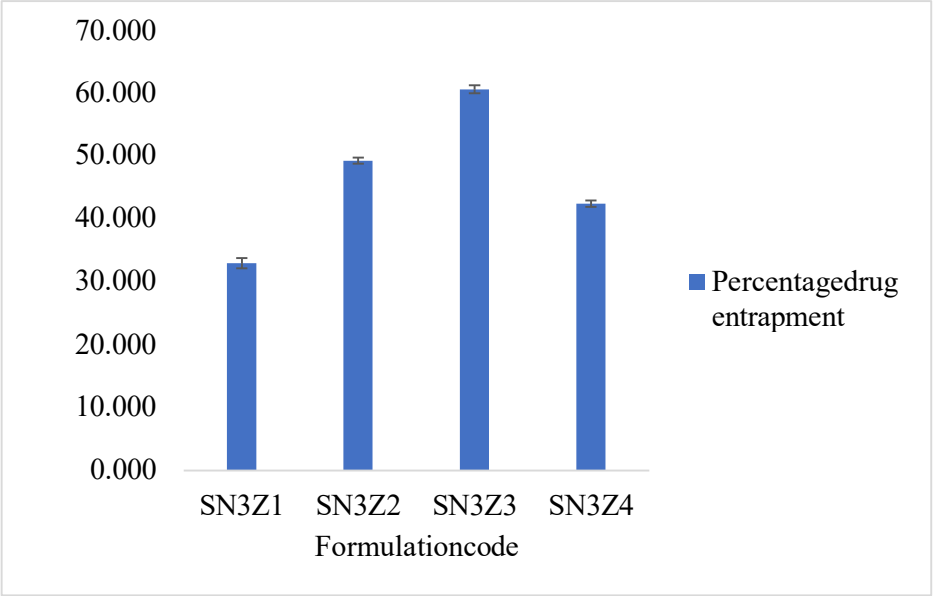


Figure3.9:%drugentrapmentofpreparedbatchesofzaltoprofenloadedsilvernanoparticle

Table3.7:%drugloadingofpreparedbatchesofzaltoprofenloadedsilver nanoparticle

S.No.	**Formulationcode**	**Percentagedrugloading**
1	SN3Z1	8.248±0.209
2	SN3Z2	24.632±0.245
3	SN3Z3	45.466±0.490
4	SN3Z4	42.443±0.510

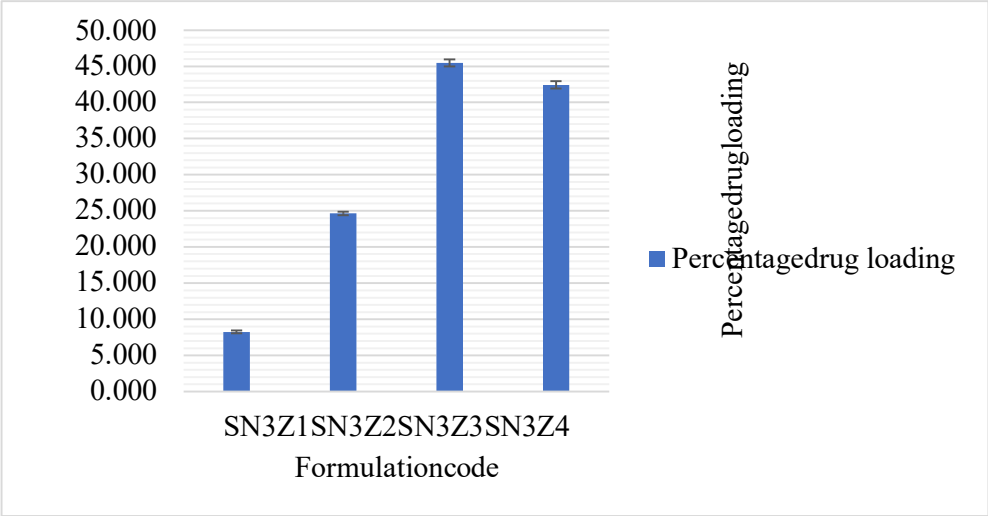


Figure3.10:%drugloadingofpreparedbatchesofzaltoprofenloadedsilvernanoparticle

3.5.3 Particlesize

The nanoscale size of formulation SN3Z3 was verified by an average particle size of 85.1 nm and PDI of 0.102, as shown in Figure 3.11. One important measure of the distribution of nanoparticlesizesisthePDI.ThechitosanlayersurroundingtheAgNPs receivesasignificant positive charge from the numerous primary amine groups in chitosan, which results in electrostaticrepulsionthatstabilizestheparticles.AgNPparticlesarelesslikelytoagglomerate into larger sizes as a result. Furthermore, because CS's primary amines have positive charges, anionic molecules can form complexes [92, 37].

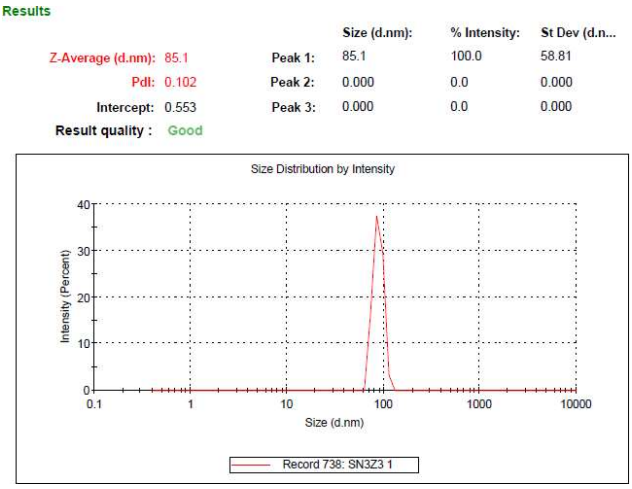


Figure3.11: ParticlesizedistributiongraphofformulationSN3Z3.

3.5.4 Zeta potential

The zeta potential measures the effective electric charge around the surface of the nano composite. It quantifies the charge differential between the ions in the surrounding dispersion media and those at the nanocomposite surface. This electric charge has a major impact on the stability behavior and toxicity of the nanomaterial.We also assess the optimum formulation's zeta-potential and particle size distribution. In this study, a dynamic light scattering (DLS) zetasizerwasusedtoassessthebestformulation'szetapotential.Theaveragezetapotentialfor theSN3Z3formulationwas23.8mV.Chitosan'saminoandhydroxylgroupsencouragebinding to silver ions.A highly stable nanoparticle dispersion with strong electrostatic repulsion that inhibits aggregation is reflected in such a

high zeta potential. Typically, zeta potential greater thanabout+25to+30mVorlessthan−25to−30mVdenoteastablenanocomposite[91,37].

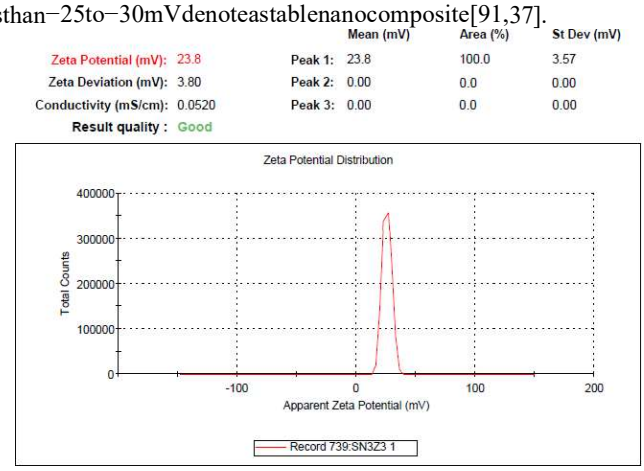


Figure3.12: Zetapotentialgraphofformulationofformulation SN3Z3

3.5.5 TEM

Transmission electron microscopy (TEM), which offers two-dimensional, high-magnification images of the nanoparticles, was used to analyze the samples. Black spherical and quasi-spherical AgNPs were seen in TEM pictures. The ChAgNPs (SN3Z3) exhibited little to no aggregation, suggesting that the particles are repulsive to one another. The chitosan–silver polymeric composite's electrostatic interactions, which produce a positively charged steric barriersurroundingthe metalcore,areresponsibleforthisrepulsion.TheaveragesizeofChi-Ag-NPs(SN3Z3)asassessedbyZetasizerisgreaterthanthatdisplayedbyTEMpictures.The several measuring conditions and concepts that were used led to this outcome. Silver nanoparticles are dispersed by coordination or ionic contacts between chitosan polymer molecules andAg-NPs without appreciably changing their morphological properties [91,97].

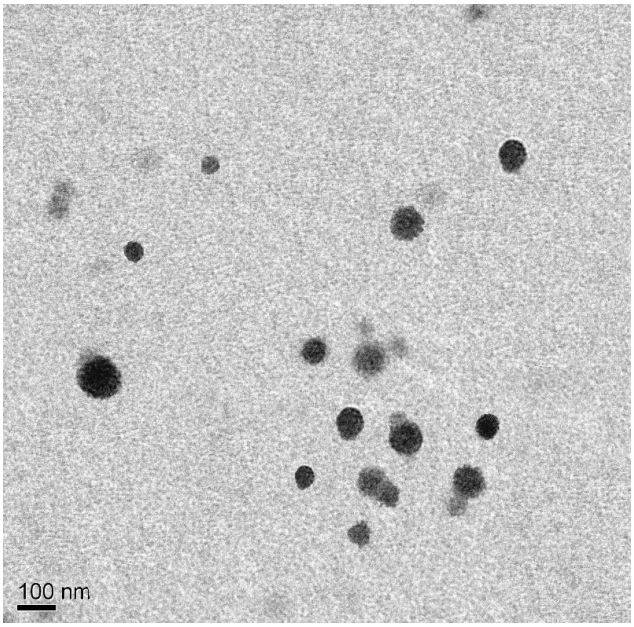


Figure3.13:TEMimagesoftheformulationSN3Z3

TheaboveinvestigationparametersconfirmedthatformulationSN3Z3wassutaibleforthegel formulation and its characterization.

3.6 Preparationofzaltoprofenloadedsilvernanoparticlegel

Theselectedzaltoprofen-loadedsilvernanoparticleformulationSN3Z3wasincorporatedinto carbopol to prepare the gel.A total of four baths of silver nanoparticle gel formulation were made, each containing a different concentration of carbopol 940 (1%w/w, 1.5%w/w, 2%w/w, and 2.5%w/w). Additional characterization was done on the obtained silver nanoparticle gel formulation loaded with zaltoprofen.

3.7 Invitrocharacterizationofthezaltoprofenloadedsilvernanoparticlegel

3.7.1 Physical appearance

The physical characteristics of each prepared batch of gel formulations, such as color, homogeneity,anduniformity,weredisplayedinTable3.17.Theobservationsverifythatevery createdformulationhadadarkyellowish-browncolor,wasuniform,homogenous,anddevoid of grit and particles. In comparison to the other formulation, the SN3Z3G1 formulation had less viscosity.

Table3.17: Physicalappearanceoftheallpreparedzaltoprofenloadedsilvernanoparticlegel

S.No.	Formulation code	Physicalappearance
1	SN3Z3G1	Darkyellowish-browncolor,homogenous,uniform,free fromparticlesandgrittiness,lessviscousgel
2	SN3Z3G2	Darkyellowish-browncolor,homogenous,uniform,free fromparticlesandgrittiness,viscousgel
3	SN3Z3G3	Darkyellowish-browncolor,homogenous,uniform,free fromparticlesandgrittiness,viscousgel
4	SN3Z3G4	Darkyellowish-browncolor,homogenous,uniform,free fromparticlesandgrittiness,viscousgel

3.7.2 pH

Table 3.18 displayed the pH observations for all produced formulations. All of the manufactured batches of zaltoprofen-loaded silver nanoparticle gel had pH values between 5.613±0.291 and 5.753±0.038, which is comparable to the pH of skin. The mixture did not cause irritation upon application since its pH fell within the normal range of the skin's pH.

Table3.18:pHofthepreparedformulationszaltoprofenloadedsilvernanoparticlegel

S.No.	Formulationcode	pH
1	SN3Z3G1	5.753±0.038
2	SN3Z3G2	5.683±0.035
3	SN3Z3G3	5.613±0.291
4	SN3Z3G4	5.773±0.050

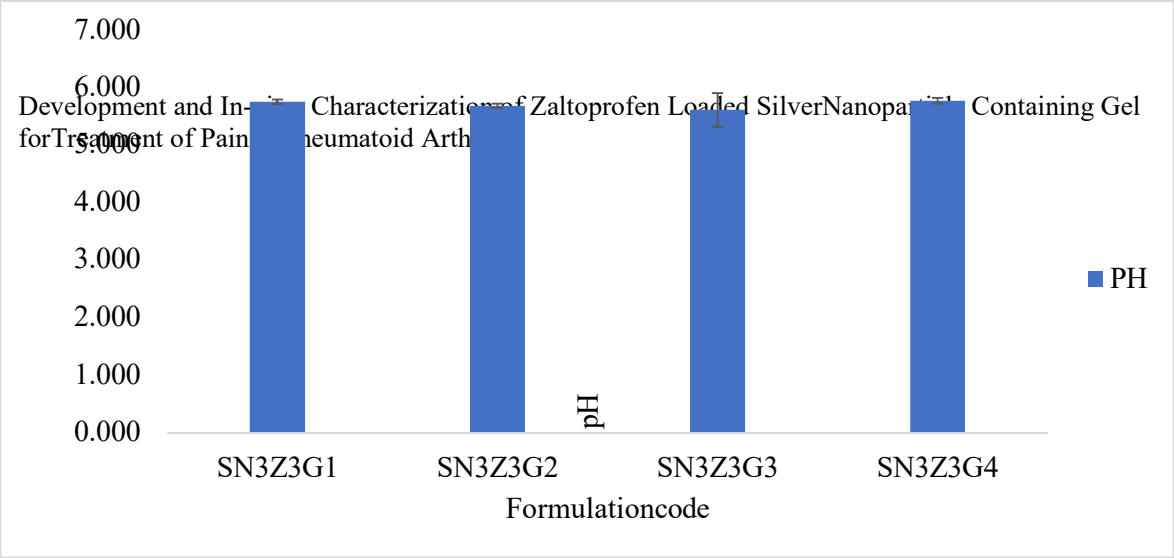


Figure3.14:pHoftheallpreparedformulationzaltoprofenloadedsilvernanoparticlegel

3.7.3 Spreadability

Table 3.19 displayed the findings of the spreadability of each manufactured gel formulation including zaltoprofen-loaded silver nanoparticles. All prepared zaltoprofen-loaded silver nanoparticle gels had spreadability ranging from 6.383±0.062 to 31.922±0.582gm.cm/sec. Resulting, the hydrogel composition becomes less spreadable as the amount of carbopol increases due to its increased viscosity. Among all the gel formulations, the 2%w/w concentration of carbopol exhibited the best spreadability out of the four distinct concentrations. It has been demonstrated that the gels have good spreadability and are simple to spread with little cutting [94].

Table3.19: Spreadabilityofallthepreparedformulations

S.No.	Formulationcode	Spreadability(gm.cm/sec)
1	SN3Z3G1	31.922±0.582
2	SN3Z3G2	13.525±0.492
3	SN3Z3G3	8.803±0.273
4	SN3Z3G4	6.383±0.062

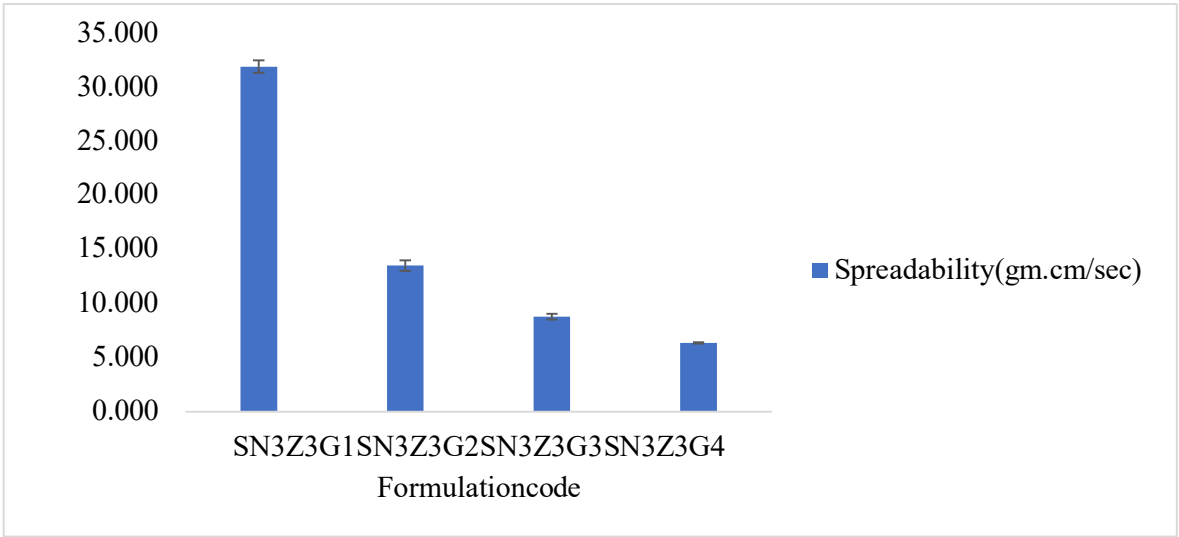


Figure3.15: Spreadabilityoftheallpreparedformulation

3.7.4 Percentagedrug content

Table7.20displaystheobservationspertainingtothepercentagedrugcontentofallgenerated silver nanoparticle gel formulations loaded with zaltoprofen. Table 7.20 shows that all formulations' drug content ranged from 95.486±0.352% to 99.775±0.708%, demonstrating good formulation uniformity [118].

Table3.20: Percentagedrugcontentofthepreparedzaltoprofenloadedsilvernanoparticlegel formulations

S.no.	FormulationCode	%drugcontent(%)
1	SN3Z3G1	95.486±0.352
2	SN3Z3G2	99.775±0.708
3	SN3Z3G3	99.367±0.936
4	SN3Z3G4	95.895±1.061

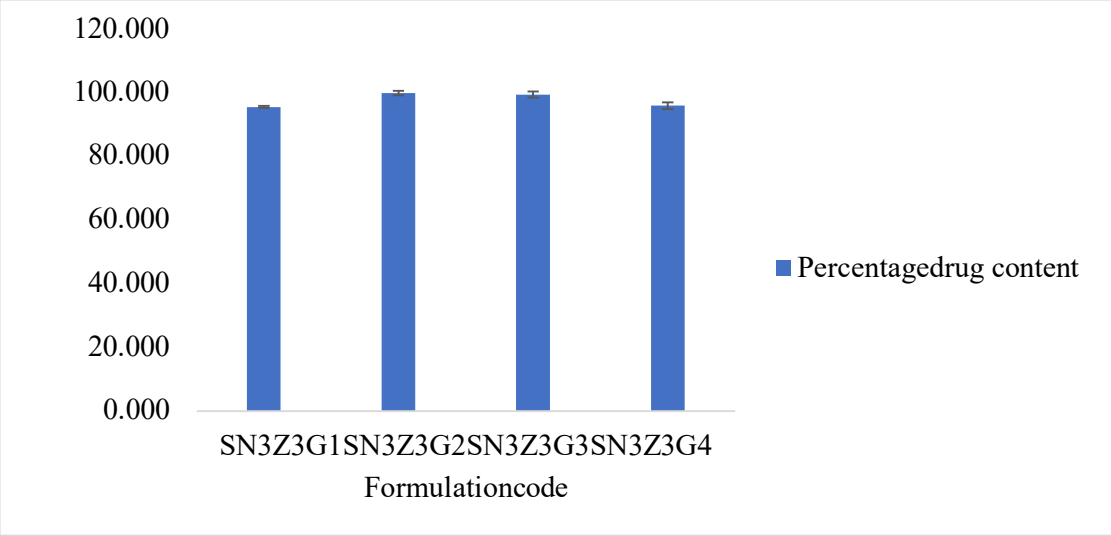


Figure 3.16: % drug content of the prepared zaltoprofen loaded silver nanoparticle gel formulations

3.7.5 Viscosity

Table 3.21 displayed the findings regarding the viscosity of all generated gel formulations including silver nanoparticles loaded with zaltoprofen. The viscosities of all the generated batches of silver nanoparticle gel

formulations loaded with zaltoprofen ranged from 1146.000±1.000cpto 5502.667±1.155cp.Thefindings showed that the viscosity increased with the concentration of the gelling agents [118].

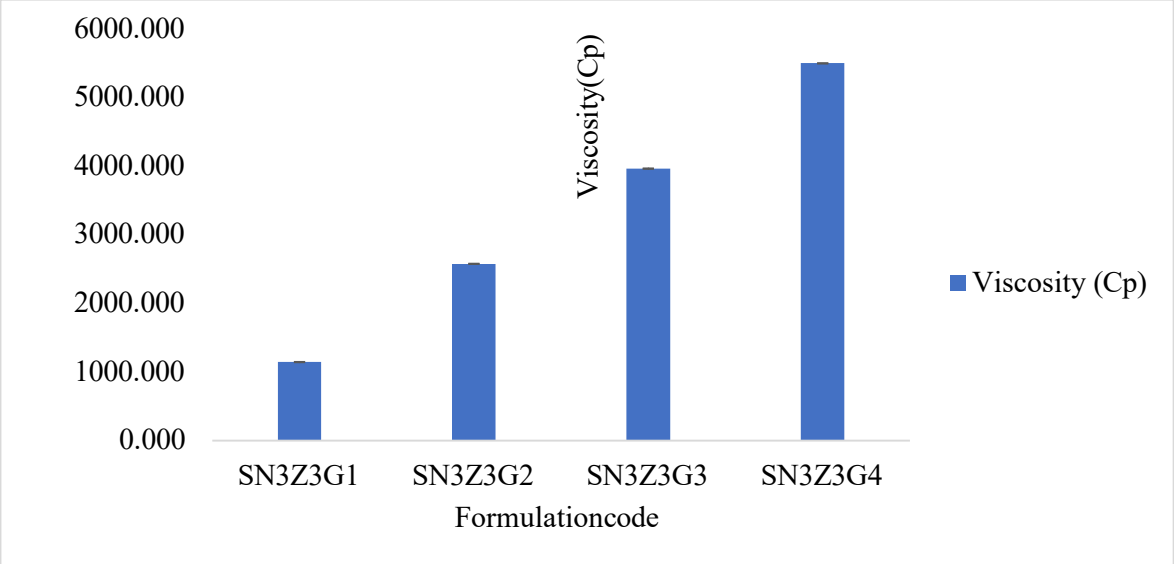


Table3.21: Viscosityofthepreparedzaltoprofenloadedsilvernanoparticlegel formulations

S.no.	FormulationCode	Viscosity(Cp)
1	SN3Z3G1	1146.000±1.000
2	SN3Z3G2	2577.667±1.528
3	SN3Z3G3	3966.667±0.577
4	SN3Z3G4	5502.667±1.155

Figure3.17: Viscosityoftheall-prepared formulation

TheobservationsoftheaboveinvestigationparametersconfirmedthatformulationsSN3Z3G2 and SN3Z3G3 were suitable for further evaluation.

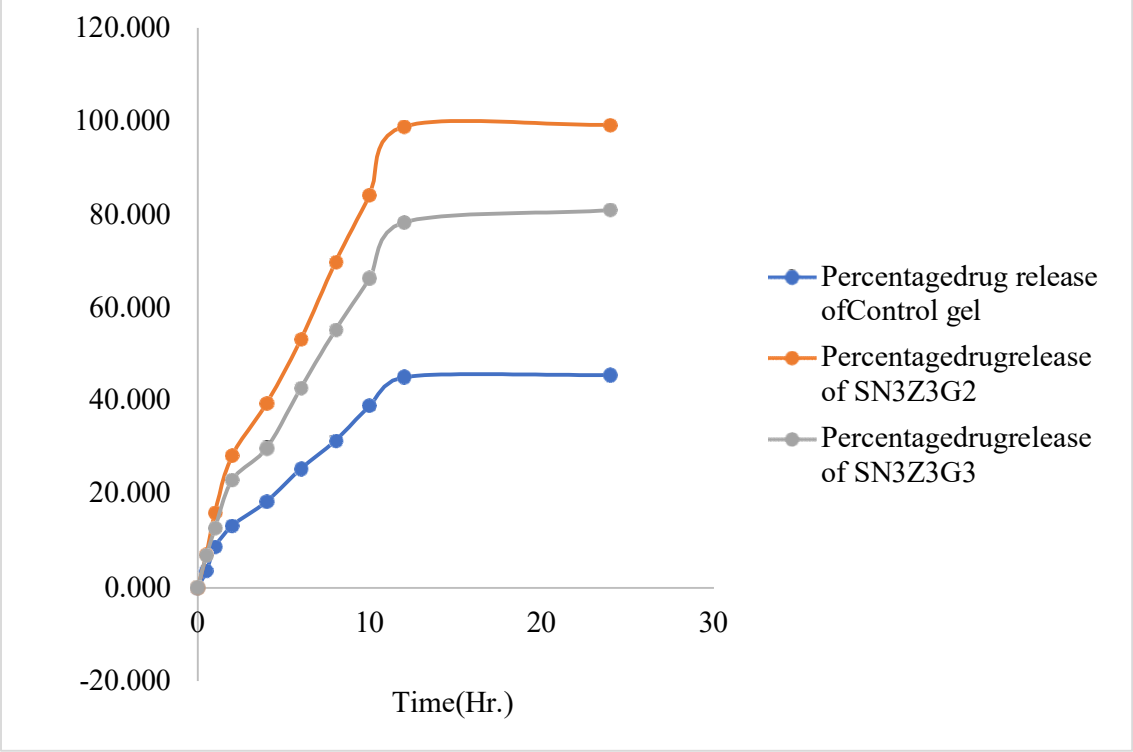
3.7.6 Percentagedrug release

The % drug release of the "zaltoprofen-loaded silver nanoparticle gel" formulations ("SN3Z3G2"and "SN3Z3G3") and "control gel"are displayed inTable 3.22.This shows that the maximum drug release at 24 hours was 45.619±0.463%, 99.173±0.318%, and 80.913±0.592 for the "control gel", "silver nanoparticle gel formulation" "SN3Z3G2", and "SN3Z3G3".Fromtheproducedsilvernanoparticle,thedrugshowedbothburstandsustained release.Interactionsbetweenthedrugmoleculesandthebionanocompositeareresponsiblefor prolonged release. When the generated silver nanoparticle matrix comes into touch with the aqueoussolution,itstartstoswell,whichcausesthedrugmoleculestodiffusefromtheporous networkof thesilver nanoparticlestothe outer medium.Adiffusion-driven mechanismreleases the medication from the silver nanoparticles [128].

Table 3.22: Percentage drug release of the zaltoprofen loaded silver nanoparticle gel formulations (SN3Z3G2 and SN3Z3G3) and control gel

S.No.	Time (hr.)	Percentage drug-releaseofControl gel	Percentage drug-release of SN3Z3G2	Percentage drug-release of SN3Z3G3
1	0	0.000±000	0.000±0.00	0.000±0.000
2	0.5	3.585±0.184	7.200±0.103	6.955±0.281
3	1	8.732±0.368	16.146±0.212	12.776±0.184
4	2	13.266±0.463	28.339±0.281	23.131±0.383
5	4	18.474±0.663	39.491±0.383	29.933±0.212
6	6	25.521±0.562	53.278±0.531	42.862±0.463
7	8	31.526±0.919	69.761±0.663	55.239±0.663
8	10	39.001±0.829	84.161±0.562	66.391±0.765
9	12	45.190±0.646	98.866±0.696	78.339±0.646
10	24	45.619±0.463	99.173±0.318	80.913±0.592

Figure 3.18: % drug-release of the zaltoprofen loaded silver nanoparticle gel formulations (SN3Z3G2 and SN3Z3G3) and control gel



3.7.7 Drug-releasekineticstudy

The in vitro drug-release profile of formulation SN3Z3G2 was analyzed using several kinetic models, including "zero-order", "first-order", "Higuchi", and "Korsmeyer–Peppas".As seen inFigures3.19-3.22,variouskineticsmodelswereutilizedtoplotdrugreleaselinearly,

yielding regression coefficient values. The values of the regression coefficient of the linear relationship between the drug releases at various times were used to evaluate drug release models.Table3.23summarizesthedrugreleaseoutcomesofvariouskineticmodels.Withthe highest regression

coefficient value (R^2 = 0.9918) [128], the drug release profile most closely matched the Korsmeyer Peppas model kinetic model.

Table3.23: Drugreleasekineticmodel

S.No.	Model	Regressioncoefficient
1	"ZeroOrder"	0.7661
2	"Firstorder"	0.8319
3	"Higuchi order"	0.9139
4	"Korsmeyer-Peppasmodel"	0.9918

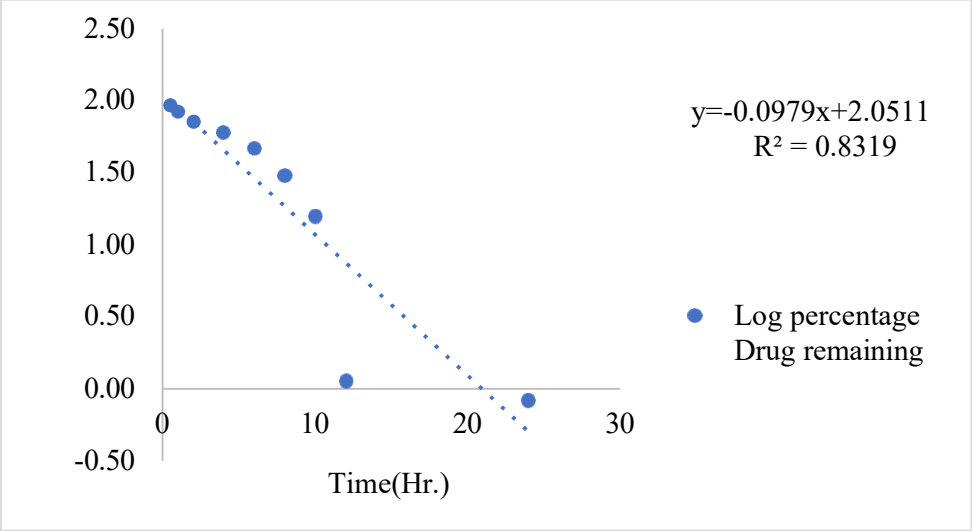


Figure3.20: Firstorder

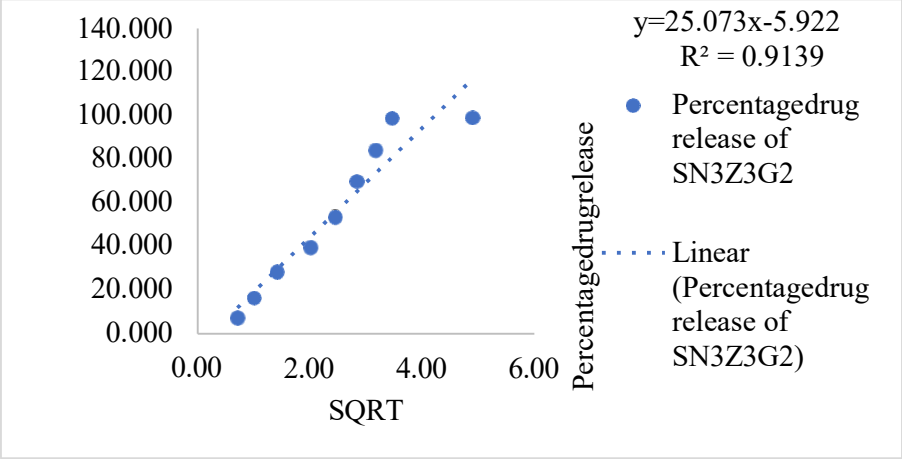


Figure3.21: Higuchi order

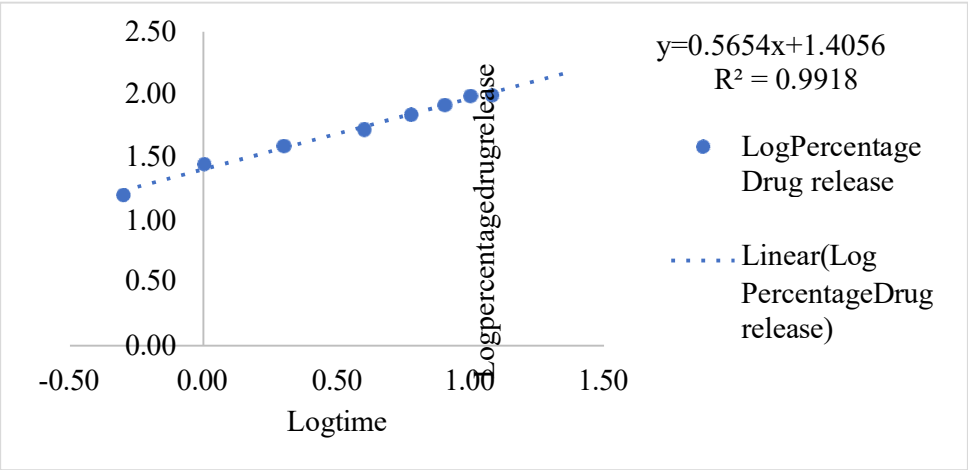


Figure3.22: Korsmeyer-Peppasorder

3.7.8 FTIR spectroscopy

The infrared spectra of the puremedication and the zaltoprofen-loaded silver nanoparticle gel (SN3Z3G2) are shown in Figures 3.23 and 3.24. The primary bands were identified, and any corresponding changes were recorded. Pure zaltoprofen has distinctive peaks in its FTIR spectrum at 939.56 cm^{-1} ("aromatic -C–S–C– stretching"), 2976.52 cm^{-1} ("carboxylic group O–H stretching"), 1330.47 cm^{-1} ("CH3stretching"), and 1699.23 and 1668.53 cm^{-1} ("carboxylic group stretching"). The zaltoprofen-loaded silver nanoparticles were uniformly distributed throughout the gel matrix in the FTIR of formulation SN3Z3G2, and the drug's distinctive peaks were less intense.

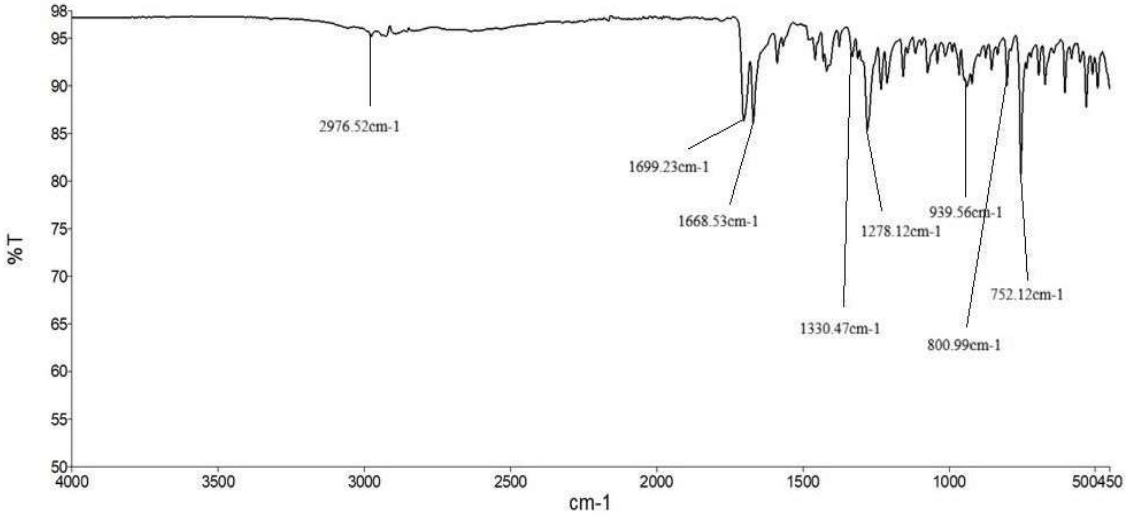


Figure3.23:FTIRspectrumof zaltoprofen

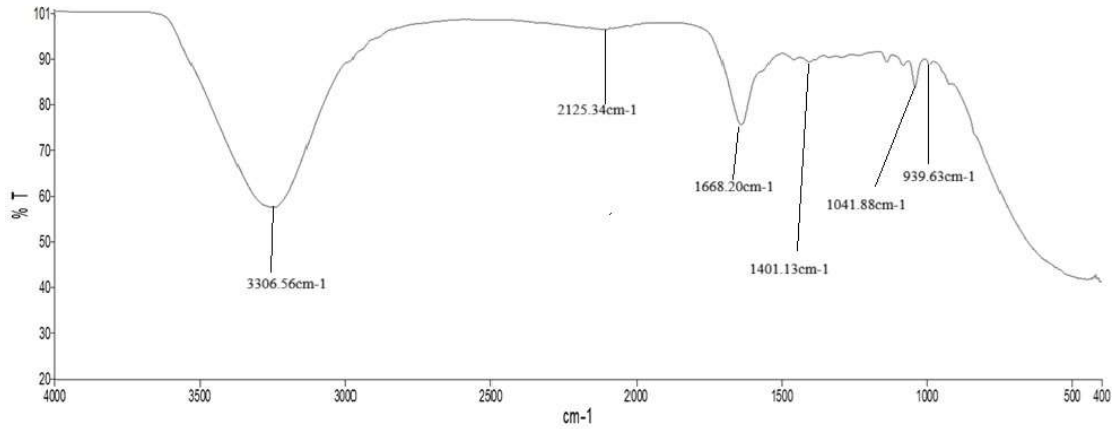


Figure3.24:FTIRspectrumofzaltoprofenloaded silvernanoparticlegel (SN3Z3G2)

4. CONCLUSION

The goal of this work was to create a silver nanoparticle gel loaded with zaltoprofen in order to enhance drug delivery for the treatment of rheumatoid arthritis. According to the preformulationresearch,zaltoprofenisawhitepowderthatistastelessandodorless.Itsmelting points were determined to be 128.33°C±0.58 and 130.00°C±1.00. Its partition coefficient of 2.525±0.013 indicated that it is a lipophilic medication. Silver nitrate was reduced to the nanoscale using sodium hydroxide and chitosan as reducing agents to create silver nanoparticles.5ml,10ml,20ml,30ml,and40mlofthe0.5%w/vchitosansolutionwereused to create the silver nanoparticle. SN1 through SN3 codes were assigned to each synthesized formulation. The produced silver nanoparticles showed good stability with a suitable zeta potential, low polydispersity index (PDI), and an optimum particle size.Positive physicochemical properties of the optimized nanoparticle gel included appropriate pH, viscosity, spreadability, and drug content.

In vitro drug release experiments demonstrated that, in contrast to the traditional formulation, zaltoprofenwasreleased fromthenanoparticle-loadedgelinasustainedandcontrolledmanner.

Silver nanoparticles are anticipated to boost Zaltoprofen's anti-inflammatory properties, offer antimicrobial defense, and improve skin penetration.The gel's formulation may improve localizeddrugdeliveryforrheumatoidarthritiswhileloweringthesystemicsideeffectsoforal NSAID therapy.

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