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FORMULATION AND EVALUATION OF PHYTOSOME LOADED DRUG DELIVERY FOR THE TREATMENT OF RESPIRATORY INFECTION

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ABSTRACT:

Aim In this formulation of the Phytosome loaded delivery with 6-ginger for the treatment of respiratory infection and evaluate the formulation of phytosome formulation of drug and also complex formulation of drugs i.e. 6-ginger. For the study of formulation evaluation parameters are shape of phytosome, FT-IR, DSR, determination of % yield, partical size and entrapment efficiency of drug and in-vitro study also.To overcome these issues and make home grown treatment more viably for the treatment of RTI, novel drug delivery (nanoparticle) based phytosome loaded complex approach was adopted.The prepared nanoparticle based complex of phytosome loaded of both phyto constituent drugs have the combined effect of chitosan and phytosome

KEYWORDS:

Phytosome, Respiratory Infection, Nanoparticle, Novel drug delivery

INTRODUCTION:

The respiratory system (called likewise respiratory device, ventilator system) is a natural system including specific organs and structures used for the methodology of take in a living being. Respiratory infections are most regularly happen in the winter season when chill, wet, clammy climate influence the working of the lungs and other respiratory organs. Respiratory tract infection (RTI) is one of the common issues, all the more particularly in kids.[1] Respiratory tract infection again delegated upper respiratory tract infection (URI or URTI) or a lower respiratory tract infection (LRI or LRTI). Lower respiratory tract infection can make a great deal of confusions like pneumonia, bronchitis, bronchial asthma and it is considerably more genuine than upper respiratory infection, for example, the common cold. Upper respiratory tract infection is much regular ailment and can be related with tonsillitis, pharyngitis, laryngitis, sinusitis, otitis media, flu, and so on.[2]In any case, normal frosty with indications like cough, sore throat, runny nose, nasal congestion, headache, low grade fever, sneezing, and so on are exceptionally hard to treat.

Extensive consideration has been centred on the advancement of novel drug delivery system (NDDS) for home grown medications in the previous couple of decades. The novel transporters ought to preferably satisfy two essentials. Right off the bat, it ought to convey the medication at a rate coordinated by the requirements of the body, over the time of treatment. Also, it should channel the dynamic substance of natural medication to the site of activity. Conventional dosage forms including prolongedrelease dosage forms can't meet none of these.[3]

Phytosome results from reaction of stoichiometric amount of phospholipid mostly phosphatidylcholine with a standardized herbal extract in an aprotic solvent. Phosphatidylcholine is a bifunctional compound, the phosphatidylmoiety being lipophilic in nature which is the head of the bifunctional compound and the choline moiety which is the tail of the bifunctional compound being hydrophilic in nature.The term “phyto” means plant while “some” means cell like. The phytosome technology produces a little micro sphere or little cell, which protects the plant extract or its active constituent from destruction by gastric secretion and gut bacteria due to the gastroprotective property of phosphatidylcholine .

MATERIAL AND METHODS:

Phytosome Formulations of Drug: As per the requirements of the molar ratio (1:1) for the formulation, the particular measure of drug and phospholipid were taken in a 100 mL round base flask and refluxed with 30 mL of methanol at a temperature not surpassing 60^0C in magnetic stirrer for 2 h followed by evaporation. The blend was concentrated to 5 mL and nhexane (20 mL) was added purposely with constant mixing to get the precipitate which was sifted, gathered and put away in vacuum desiccators for overnight. Powdered phytosome formulation was set in golden shading glass bottle and stored at room temperature.

Phytosome Loaded Complex Formulations of Drug: As per the requirements of the molar ratio (1:1:0.25) for the formulation, the particular measure of drug and phospholipid were taken into a 100 mL round base flask and refluxed with 30 mL of methanol at a temperature not surpassing 60^0C in magnetic stirrer for 2 h followed by evaporation. The blend was concentrated to 5 mL at that point and n-hexane Materials and Methods 31 (20 mL) was additionally added precisely with ceaseless mixing to get the precipitate. The precipitate was introduced drop wise (0.2 mL/min) into 2% acetic acid (v/v) solution of chitosan (0.25 % w/v) toget the complex formulations using magnetic stirrer with expanding the temperature above 60^0C. The precipitate was sifted, gathered and put away in vacuum desiccators for overnight. Powdered drug loaded phytosomecomplex formulation was set in golden shading glass bottle and placed at room temperature.[4-6]

Shape of the phytosome:

Optical microscope was used for the characterization of the formulations. The formulation was suspended in phosphate buffer pH7.4 and a drop was set on a slide and secured with a cover slip. Microscopic view of the complex was observed at amplification of 10x10.[7-8]

Characterization, Evaluation and Optimization of final batch of phytosome andphytosome loaded complex:

The phytosome and complex of phytosome loaded formulations of drug were characterized by FT-IR and DSC for compatibility and evaluated for % yield, % entrapment efficiency, % drug loading, particle size and in vitro drug release and stability studies to get the optimize formulation.

FT-IR compatibility study:

The prepared phytosome and complex of phytosome loaded formulations of drug were characterized using FT-IR Spectrophotometer (Shimadzu-8400S, Tokyo, Japan) by KBr pellet method.[9]

Differential Scanning Calorimetry (DSC) study:

The prepared phytosome and complex of phytosome loaded formulations of drug were characterized by Differential scanning calorimeter (Shimadzu DSC60, Japan) using Aluminium pans.[10]

Determination of % yield:

Assurance of % yield of formulations was calculated by the accompanying equation:[11]

(%) Yield = Practical yield × 100 Theoretical yield

Determination of particle size:

The mean diameter of formulations were estimated by dynamic light scattering (DLS) using particle size analyser (Zetasizer 2000, Malvern Instruments Ltd., UK) at a settled scrambling point of 90o at 25o C. The analysis was performed thrice and the average hydrodynamic particle size was expressed as the value of z-average size ± SD.[12]

Determination of entrapment efficiency and drug loading:

The entrapment efficiency and drug loading of formulations were dictated by centrifugation method (RemiElektroTechnik Ltd, Vasai, India). The prepared formulation was vortexed and centrifuged with 10 mL of methanol at 5000 rpm for 10 min. The free amount of the drug in the filtrate was determined by UV/Vis spectroscopy (Shimadzu-1800, Japan) at 280 nm for gingerol and 326 nm for cuminaldehyde, respectively. The weight of the formulation was determined after the completion of experiment through weighing in the form of practical yield. Estimations were

performed in triplicate. The entrapment efficiency and drug loading was figured by the accompanying formula:[13]

Entrapment efficiency (%) = Total amount of drug – amount of free drug × 100 Total amount of drug Drug loading (%) =Weight of the drug in the Formulation × 100 Weight of the Formulation

In vitro drug release:

On the basis of literature survey and the target route for the therapeutic activity was orally, 0.01 M phosphate buffer pH 7.4 (900 mL) was utilized as a dissolution medium for 24 hours and maintained at 37 ± 0.5°C. Dissolution study was completed utilizing dissolution apparatus (Electro lab TDT-08L, Mumbai) by USP II paddle method at 50 rpm. The cotton tea filter bag 0.1µm pore size was utilized to complete the in vitro drug release. A 100 mg dose of powdered sample was filled in separate cotton tea filter bags and dipped into jar containing medium and it was closed with cover to avoid vanishing of the dissolution medium. At predetermined time intervals (0, 0.5, 1, 2, 3, 4, 5, 6, 8, 12 and 24 h), aliquots were withdrawn and displaced with the similar measure of phosphate buffer. The sample was assayed by UV spectrophotometer (Shimadzu-1800, Japan) at 276 nm for gingerol and 249 nm for cuminaldehyde, respectively and calculated from the standard calibration curve. The experiment was repeated three times and the values recorded as mean ± standard deviation (SD).[14]

In vitro Antioxidant Study:

Oxygen utilization fundamental in cell development, prompts the age of a progression of responsive oxygen species. They are consistently created by the body's typical utilization of oxygen, for example, breath. Because of increment of free radical age ordebilitated endogenous cell reinforcement system (oxidative pressure) is an imperative factor that has been worried in different illnesses. The reactive oxygen species incorporate, for example, superoxide anion radicals, and hydroxyl radicals and without non radical's species, for example, hydrogen peroxide. Reactive oxygen species are consistently delivered amid ordinary physiologic occasions and can without much of a stretch start the peroxidation of layer lipids, pivotal bimolecular, for example, nucleic acids, proteins and sugar. Antioxidant can keep in defend position of the human body from free radical and reactive oxygen species impact. They back off the advance of

numerous interminable diseases. Subsequently, requirement for distinguish elective regular and safe wellspring of food neutraceuticals.[15]

RESULT:

In Fig. 1(1) The preliminary batches of **phytosome and phytosomeloaded complex** formulations of gingerol was prepared by different methods. The quantitative results indicate that phytosome of gingerol obtained from various methods. It was found that the anti-solvent precipitation method showed 63.96±0.02 % yield, 565.19±0.48 nm particle size, 87.05±1.20 % entrapment efficiency and 04.66±0.30 % drug loading as compare to 86.88±1.01 % yield, 663.06±0.05 nm particle size, 71.28±0.03 % entrapment efficiency, 14.12±0.70 % drug loading by solvent evaporation, 76.75±0.05 % yield, 779.89±0.31 nm particle size, 40.88±0.21 % entrapment efficiency, 10.88±0.21 % drug loading by rotary evaporation technique and 74.62±0.90 % yield, 658.01±0.53 nm 60 particle size, 82.16±0.22 % entrapment efficiency, 09.65±0.68 % drug loading by anhydrous cosolventlyophilization.

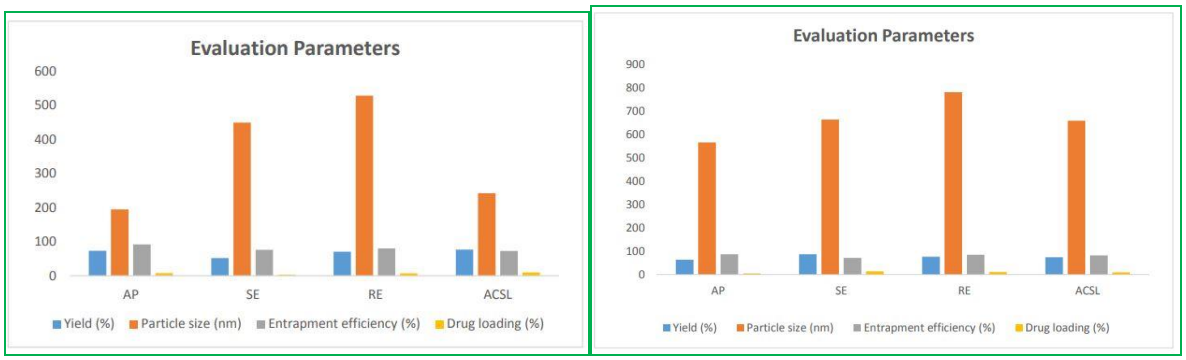


Fig1-(1)Evaluation of preliminary batches of gingerolphytosomes (2)Evaluation of preliminary batches of gingerol loaded phytosomes.

It was found that the anti-solvent precipitation method showed 73.70±0.12% yield, 94.85±0.77 nm particle size, 92.23±0.07 % entrapment efficiency and 08.34±0.90 % drug loading as compare to 52.32±0.62 % yield, 448.98±0.01 nm particle size, 76.37±0.31 % entrapment efficiency, 03.19±0.03 % drug loading by solvent evaporation, 70.97±1.03 % yield, 527.90±0.82 nm particle size, 80.06±0.29 % entrapment efficiency, 07.74±0.79 % drug loading by rotary evaporation technique and 76.88±0.94 % yield, 242.01±0.67 nm.

In Fig. 1 (2)The optimized phytosome of gingerol GP4 was characterized by **FT-IR**spectrum as shown in Fig 2. A shift from 3429 cm-1 to 3418 cm-1 and 2927 cm-1 to 3429 cm-1 compared to gingerol and a shift from 1733 cm-1 to 1731 cm1 compared with soya lecithin were exhibited by optimized phytosome of GP4. These changes confirmed the formation of phytosome by the hydrogen bonding between the –OH group of phenolic ring of gingerol and P=O group of soya lecithin.

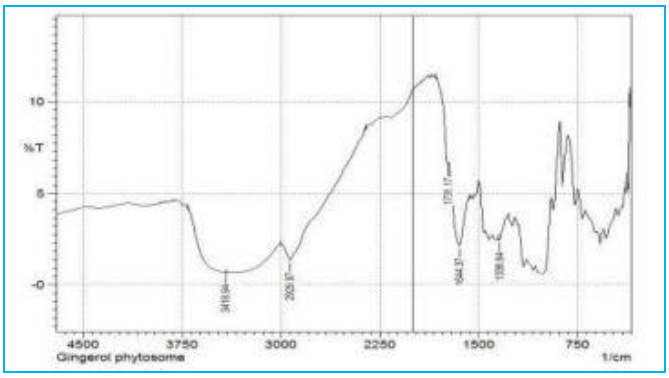


Fig 2 IR spectrum of Optimized Gingerolphytosome (GP4)

Particle size, 73.10±0.72 % entrapment efficiency, 09.83±0.47 % drug loading by anhydrous co-solvent lyophilization.

The **in vitro cumulative**gingerol release from phytosome (GP1-GP5) is given in figure 3. It showed that highest 86.03±0.06 % cumulative drug release of GP4 at the end of 24 h.

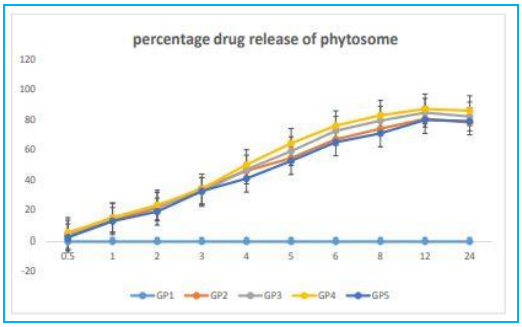
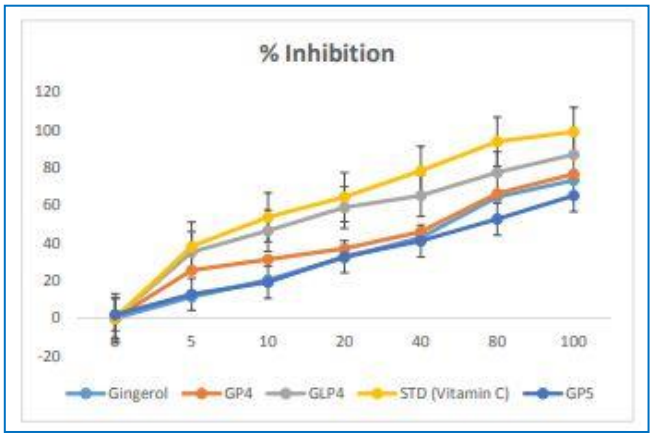


Fig. 3 In vitro cumulative drug release of phytosome of gingerol

In vitro Antioxidant StudyDPPH Assay: In fig 4(1) The optimized GLP4 showed the maximum scavenging activity (Lowest IC50 = 17.70±0.10 µg/mL) followed by optimized GP4 (IC50 = 46.23 ±0.06 µg/mL) and gingerol (IC50 = 57.74 ±0.02 µg/mL). Vitamin C was used as a reference, showed lowest (IC50 = 05.51± 0.07 µg/mL)

scavenging activity as compared order of GLP4 > GP4 >gingerol. Reference Vitamin C and optimized GLP4 showed a dose dependent inhibition on the DPPH radicals.

Hydrogen peroxide Assay: In fig 4(2) The optimized GLP4 showed the maximum scavenging activity (Lowest IC50 = 19.46 ± 0.06 µg/mL) followed by optimized GP4 (IC50 = 40.48± 0.40 µg/mL) and gingerol(IC50 = 53.52±0.02 µg/mL). Vitamin C was used as a reference,showed lowest (IC50 = 06.08± 0.01 µg/mL) scavenging activity as compared order of GLP4 < GP4 >gingerol.



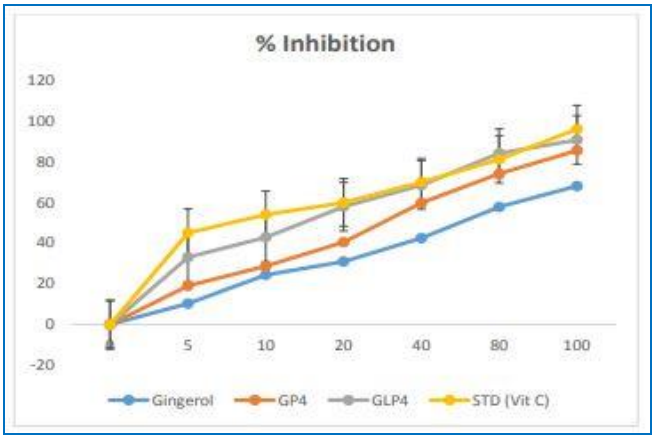


Fig 4(1) DPPH Assay of Gingerol (2) H2O2 Assay of Gingerol

The results of **stability study** of the optimized gingerolphytosome (GP4) and Gingerolphytosome loaded complex (GLP4) after 0 month, 1 month, 2 months and 6 months at different storage conditions. Comparison of both GP4 and GLP4. At predetermined intervals (0 month, 1 month, 2 months and 6 months), there was a slight increase in mean particle size and decrease in % EE & % DL of GP4, when it was stored at 4˚C and at room temperature (25 ± 2˚C/ 60 ± 5 % RH). But, At 45 ± 2˚C/75 ± 5% RH, GP4 was shown the significant increase in mean particle size and decrease in % EE & % DL after 2 and 6 months, indicated the high temperature can lead to aggregation and sedimentation of the particles after a period of time and also suggested that the phyto-constituent or gingerol gets degraded at that temperature hence may decrease the drug release of the GP4. In case of GLP4, at different temperature storage conditions (4˚C, 25 ± 2˚C & 45 ± 2˚C), it was showing insignificant alteration on mean particle size and % EE & % DL after 2 and 6 months, due to compatible interaction of gingerol with soya lecithin and chitosan. Therefore, in vitro stability study of optimized

GLP4 verified the interaction of gingerol with soya lecithin phospholipids that protected by the chitosan against the degradation.

DISCUSSION:

Respiratory tract infection (RTI) is a standout amongst the most well-known issues and happens in the winter season when cool, wet, moist climate influence the working of the lungs and other respiratory organs. It transmits from individual to individual, particularly in youngsters. Fortunately, helpful home grown medications can affect respiratory sufferings. The phyto-constituent antibacterial drugs Gingerol exhibits low bioavailability, poor water-solubility and is rapidly eliminated from the body. To overcome these issues and make home grown treatment more viably for the treatment of RTI, novel drug delivery (nanoparticle) based phytosome loaded complex approach was adopted.

CONCLUSION:

The prepared nanoparticle based complex ofphytosome loaded of both phytoconstituent drugs have the combined effect of chitosan and phytosome which shown significant sustained-release profile and also prolonging the oral absorption rate of drug with effective antibacterial activity in a better stable way at different storage conditions than phytosome or drug with chitosan.

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