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Novel Formulation and Assessment of Oral Dissolving Film Incorporated with *Radix Bupleuri* Silver Nanoparticles to Treat SARS COVID-19 Viral Strains

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Abstract: ***Silver nanoparticles, also referred to as AgNPs, gaining particular significance at the moment as nanotechnology explores a number of interesting molecular techniques in the field of material sciences. Silver nanoparticles have become an effective new antimicrobial agent with improved efficacy with an inherent limitation of inducing toxicity to living tissues. This work will give an idea for researcher at developing Radix bupleuri silver nanoparticles, its characterization and subjected to various evaluation like visual examination, UV Visible spectral analysis, FTIR Spectroscopy, SEM analysis, TEM analysis and antiviral study. The Oral dissolving Film is prepared using Polyethylene glycol polymer and the characterized silver nanoparticles are incorporated to the above developed Polyethylene glycol oral dissolving film and evaluated for anti-microbial activity against COVID-19 viral strains. This work aids researchers in doing research in the synthesized Radix bupleuri silver Nanoparticles incorporated in a Polyethylene glycol oral dissolving film for a promising efficiency against COVID- 19 viral strains.***

Keywords: *Radix bupleuri* silver Nanoparticles, Oral dissolving film, Saikosaponin, Anti-viral activity

1. Introduction

The synthesis of NPs with different chemical compositions, sizes, and morphologies and controlled disparities is an important area of research in nanobiotechnology. Nanobiotechnology has emerged as an elementary division of contemporary nanotechnology and an untied novel approach in the fields of material science, receiving global attention due to its ample applications. It is a multidisciplinary approach resulting from the investigational use of NPs in biological systems. The use of nanotechnology and nanoparticles in commercial applications has seen a sharp rise in interest. The health industry is under major difficulty as a result of rising antibiotic resistance among microorganisms in recent years. Due to their enormous surface to volume ratio, which assures a broad spectrum of assault on microorganisms, nanoparticles have shown to be a promising choice for antimicrobial substances. Silver is a highly powerful antimicrobial agent and one of the most promising nanoparticles. The antimicrobial capacity of silver nanoparticles has been the subject of several studies. AgNPs showed notable antimicrobial properties.

Green Synthesis:
B. Chinese's root, commonly referred to as Radix Bupleuri. This study aims to use the root extract of *Radix bupleuri* a member of Apiaceae family used for the green synthesis of silver nanoparticles. This is a medicinal plant and is used for the treatment of influenza, fever, inflammation, malaria, menstrual disorders, and hepatitis. The aqueous *Radix bupleuri* extract is used in the synthesis of various nanoparticles such as gold, silver, zinc oxide etc. The important phytochemical constituents in *Radix bupleuri* are saikosaponin and flavanones which plays a vital role in producing antiviral and stability activity respectively. The aqueous *Radix bupleuri* root extract reduces silver salt by silver nitrate, this capped nanoparticle with neem extract exhibit antiviral activity.

Prior to recent developments, toxic and risky chemicals were employed in the extraction process. Thus, "green synthesis" refers to the employment of environmentally benign technologies for the production of silver nanoparticles. Green synthesis is chosen over traditional synthesis because it uses a single-step, cost-effective process that is simple to scale up for large-scale synthesis and doesn't use harmful chemicals, high pressure, or high temperatures. For the manufacture of silver nanoparticles, several studies have reported using materials such plant leaf extract, root, stem, bark, leaf, fruit, bud, and latex, as well as fungus, bacteria, and enzymes.

Advantages of green synthesis are favourable to the environment. Scale up easily for large-scale nanoparticle creation. No requirement for heat, pressure, energy, or hazardous chemicals. Less complex culture maintenance procedures are more advantageous than using the microorganism. Decrease in the price of the medium used to cultivate microorganisms.

Disadvantages of green synthesis are Genetic engineering cannot be used to transform plants into the preferred nanoparticle through optimised synthesis. Low yields of secreted protein are produced by plants, which slows the pace of synthesis.

Synthesis of Silver Nanoparticles:
Silver nanoparticles are tiny silver particles, ranging in size from 1 to 100 nm. Some materials, although being widely referred to as "silver," include a significant amount of silver oxide due to the enormous proportion of surface to bulk silver atoms. Ionic silver has a lengthy history and was first

employed to yellow-stain glass, similar to gold nanoparticles. There is now work is being done to include silver nanoparticles into a variety of medical products, such as surgical masks, bone cement, and other items. Ionic silver has also been demonstrated to be effective in curing wounds when used in the proper dosages. In fact, silver nanoparticles have taken over from silver sulfadiazine as the preferred method for treating wounds.

The antimicrobial effect of silver nanoparticles has been used to control antimicrobial growth in a variety of applications. The extreme toxicity of silver ions and silver-based compounds to microbes is well recognised. When silver nanoparticles are introduced into microbes' cells, they can cause significant structural and morphological alterations that may result in cell death. Scientists have shown that the persistent release of free silver ions from the nanoparticles, which act as a transport for silver ions, is the primary cause of the antimicrobial activity of silver nanoparticles.

Methods of Extraction:

1) Physical Method (Evaporation, Condensation)
2) Chemical method (Reduction by organic or inorganic reducing agents)
3) Biological method (Green synthesis using gold, silver, zinc and iron NPs)

Objective of the Study:

This research work is intended with Saikosaponin, a substance derived from *Radix bupleuri*, will be combined with the oral dissolving film in order to target the COVID-19 viral strain.

2. Methods and Materials

The review was based on writing searches conducted in PubMed, PubMed focused, google scholar article researcher, and the science trap. The associated key phrases were used to search through information databases for "saikosaponin, " as well as to hunt for relevant articles on the drug's usage as an immunosuppressant for respiratory illnesses and as a therapy for the coronavirus.

Plant Profile:

Plant Name: *Bupleurum chinense*
Root Name: *Radix bupleuri*
Taxonomical Classification:
Kingdom: Plantae
Clade: Tracheophytes
Clade: Angiosperms
Clade: Eudicots
Clade: Asterids
Order: Apiales
Family: Apiaceae
Genus: Bupleurum
B. chinense is the speciesthe scientific name Bupleurum chinense
Phytochemical constituents:
Polyacetylenes and saponins/triterpenoids, flavonoids are found in Bupleurum chinense roots, sometimes referred to as Radix Bupleuri.

Polymer Profile:

Name: Poly ethylene glycol 400.
Synonym: PEG400.
Molecular weight: 380-420 Daltons.4 to 8 °C (39 to 46 °F; 277 to 281 K) is the melting point.1.128 g/cm3 for density. PEG 400 is soluble in a wide range of solvents, including water, acetone, alcohols, benzene, glycerine, glycols, and aromatic hydrocarbons. Aliphatic hydrocarbons are only marginally soluble in PEG 400.

Form: LIQUIDClear and colourless, Water-soluble. A stable state. Strong oxidising agents, bleach, perchloric acid, nitric acid, alkali nitrates, and calcium oxide are incompatible.

Excipient Profile:

Name: Silver nitrate
Synonyms: Silver (1+) salt nitrate
Chemical Name: Ag No3
Weight in molecules: 169.872
Colour: white
Odour: Less strong odour
4.35 g/cm3 of density, 209.7 °C is the melting point.
Heating point: 440 C
Storage range: 2 to 8 C
Soluble in: Water, acetone, ammonia, ether, and glycerol.
Uses: Silver nitrate is an anti-infective cream that is used for the treatment of skin burns and wounds.

Safety: Headache, wooziness, nausea, and vomiting are all possible side effects of exposure to silver nitrate. to carry oxygen, resulting in methemoglobinemia, which causes headaches, tiredness, vertigo, and blue lips and skin. High exposure levels can result in breathing difficulties, collapse, and even death.

3. Experimental Methodology

1) Collection, Processing, and Extraction of *Radix bupleuri*

Radix bupleuri is a root of *Bupleurum chinense*. The *Radix bupleuri* should be collected and washed off to remove impurities and dirt. The root was cut into small pieces and extraction is done for 20mins in Soxhlet apparatus by using water.
Preparation of 1mM silver nitrate solution:

Silver nitrate solution of 1mM was prepared by adding 0.1699 of silver nitrate to 1L of distilled water.

2) Preparation of *Radix bupleuri* Silver nanoparticles:

The root should be finely cut and 20g it should be boiled in 100mL water for 20mins and filtration is done to obtain *Radix bupleuri* root extract. The extract of *Radix bupleuri* 5mL should be mixed with 45mL of 1mM silver nitrate with a 150 rpm in magnetic stirrer and change in colour indicates the formation of AgNPs.

3) Characterisation of *Radix bupleuri* silver nanoparticles:

a) UV VISIBLE SPECTROSCOPY of *Radix bupleuri* silver nanoparticles:
Based on the impact of UV light's surface plasmon resonance on nanoparticles, the formation of nanoparticles will be observed. The formation of silver nanoparticles in the solution induces the development of colour, which attributes to the distinctive surface plasmon vibrations of the corresponding nanoparticles. The absorbance maxima were obtained by UV visible Spectra Analysis.

b) FTIR analysis of *Radix bupleuri* silver nanoparticles:
Using an FTIR spectrophotometer, silver nanoparticles and their physical combination will be subjected to Fourier-Transform Infrared (FTIR) examination. A weighed quantity of the medication should be combined with PEG 400 (polymer), and their FTIR will be measured for drug polymer interaction.

c) SEM Analysis of *Radix bupleuri* Silver Nanoparticles:
The scanning electron microscopy analysis of *Radix bupleuri* silver nanoparticles in powdered form should be observed at different magnitudes 5500x, 950x.

Liquid sample is not possible to analyse in SEM so aqueous extract is made to be stirred for certain minutes and should take superannuated liquids and again stirring process is continued and finally pellets is obtained and washed with ethanol and SEM analysis is carried out.

d) TEM Analysis of *Radix bupleuri* silver nanoparticles:
The Transmission electron microscopy analysis of *Radix bupleuri* silver nanoparticles in liquid form will be observed at different magnitudes 10000x, 5500x, 950x.

4) Anti-viral Studies of *Radix bupleuri* silver nanoparticles:
The Antimicrobial Properties of *Radix bupleuri* AgNPs can be carried out against Covid-19 viral strains by using the ELISA test (or) the antiviral activity of the *Radix bupleuri* silver nanoparticle will be determined using Neutralisation assay, an assay that measures the inhibition of cytopathic effect on cell culture. (or) dye uptake methods can also be used to check the anti-viral activity. *In-silico* can also be performed for Anti-viral activity on computer or via Computer simulation.

5) Preparation of Oral dissolving film:
By using solvent casting method oral dissolving film are prepared. Excipients are added with suitable solvent and mixture of solvent is obtained and heated at 60 degree Celsius with 1000rpm. Then the excipient solvent solution is added with the polymer with 1000rpm and cooled to room temperature.

Finally, API (*Radix bupleuri* silver nanoparticles) is added to it and solvent evaporation replenishment. At the end film forming solution is obtained. By defoaming the film at 60 degree Celsius the polymer film will be obtained.

Table 1: Components needed for formulation of Oral dissolving Films.

Components	Name of components	Percentage
API	*Radix bupleuri* silver nanoparticles	30-37%
Disintegrant	Micro Crystalline	1-2%
Plasticizer	Poly ethylene glycol 400	27-30%
Sweetening agents	Mannitol	6-9%
Saliva stimulating agent	Citric acid	6-9%
Flavouring agent	White vanilla	15-18%
Colouring agent	Titanium oxide	1%

6) Evaluation of Oral dissolving film incorporated with *Radix bupleuri* silver nanoparticles:
The formulation's quality is assessed when the oral dissolving films are created.

a) Surface pH test:
By putting a layer on the 1.5% w/v agar gel surface, the surface pH may be measured. The pH of the film may be measured using the pH paper, and a change in colour shows the pH.

b) Transparency:
A simple UV spectrophotometer may be employed to measure the transparency of the film. Film samples should be positioned within the spectrophotometer cell in rectangles that have been cut off. The evaluation of a film's 600 nm transmittance. The following calculation was used to calculate the transparency of the films: Transparency is equivalent to (logT600) /b = C. The transmittance is T600. At 600 nm, b indicates the film's thickness (in millimetre), and c indicates its concentration.

c) Assay:
The content uniformity is used to calculate the amount of API in each film, and the pharmacopoeia specifies an 85-115 percent maximum.

d) Disintegration time:
There is no set time restriction for oral dissolving films, however it should dissolve in between 5 and 30 seconds.

e) Dissolution test:
The sink conditions and API dose will be the main factors considered while choosing the dissolving media. Basket or paddle dissolution device used to perform dissolution test.

f) Physical Properties:
- Thickness is measured using vernier calliper at all corners of the oral dissolving film.
- Dryness test (dry to touch, dry to handle, dry to recoat, dry to print free) a piece of paper is used and pressed into contact with the oral dissolving film. This can also be carried out by using some instruments.
- Folding endurance: by repeatedly folding for several times till breaking folding endurance is founded.

7) Anti-viral Studies of Oral dissolving film incorporated with *Radix bupleuri* silver nanoparticles:
The Antimicrobial Properties of Oral dissolving film incorporated *Radix bupleuri* AgNPs can be carried out against COVID-19 viral strains. Any type of study can be

done to evaluate the anti-viral property of the Oral dissolving film incorporated with *Radix bupleuri* AgNPs.

4. Results and Discussion

Initially the *Radix bupleuri* root will be collected, processed, and extraction is done. The 1mMcolourless silvernitrate solution will be prepared when it mixed with the *Radix bupleuri* extract it changes to pale brown. Keep on mixing the silver nitrate in *Radix bupleuri* extract it will change to dark brown. Standard graph of *Radix bupleuri* silver nanoparticles will be estimated using UV spectrophotometric method by measuring the absorbance at specific wavelength using deionized water. It must have to obey the Beer's Lamberts law and the correlation coefficient should be 0.99. The calibration curve of *Radix bupleuri* should be linear graph following the Beer's Lamberts Law. The compatibility between the silver nanoparticles and PEG 400 should be evaluated using FTIR method. There should be no appearance or disappearance of peaks in the silver nanoparticles-polymer PEG400, which confirm the absence of chemical interaction between the silver nanoparticles and PEG400. Various Oral dissolving film with varying the composition quantity should be prepared. Best formulation is selected by seeing the good texture and efficacy by comparing various formulations. SEM image of Oral Dissolving Film with *Radix bupleuri* silver nanoparticle is analysed and TEM image of Oral Dissolving Film with *Radix bupleuri* silver nanoparticle is also analysed the particle size should be in 10-110 nanometre. Various evaluation of the oral dissolving film such as surface pH, Transparency, assay, Disintegration time, Dissolution time, and physical parameters is done and stability of the film should be determined by evaluation. Different types of Anti-viral studies of *Radix bupleuri* silver nanoparticles incorporated in the oral dissolving film should be done in order to determine the antiviral activity of the formulation.

5. Summary and Conclusion

A fast-expanding scientific discipline for creating and developing gadgets is nanobiotechnology. The creation of NPs with various chemical compositions, sizes, and morphologies is a significant field of research in nanobiotechnology. The exploratory use of NPs in biological systems led to a multidisciplinary approach including the fields of biology, biochemistry, chemistry, engineering, physics, and medicine. Microbes are becoming increasingly resistant to antimicrobial agents, which poses a severe danger to the health sector. Given that they can assault a wide range of viral surfaces thanks to their high surface-to-volume ratio, nanoparticles have emerged as a promising choice for antimicrobial agents. Silver is one of the most promising nanoparticles that functions as a potent antimicrobial. For the green synthesis of silver nanoparticles, the root extract Radix bupleuri of a plant in the Apiaceae family is being employed. It is a medicinal herb that is used to cure viral ailments. Radix bupleuri extract in aqueous form is used in synthesis of variety of nanoparticles, including gold, zinc oxide, silver, and others.

The experiment's main goal is to create and evaluate an oral dissolving film that contains environmentally friendly green synthesized Radix bupleuri silver nanoparticles.

The UV spectrophotometric approach will be used to determine the standard graph of *Radix bupleuri* silver nanoparticles by measuring the absorbance at a certain wavelength using deionized water. The Beer's Lamberts rule must be followed, and the correlation coefficient must be 0.99. *Radix bupleuri*'s calibration curve should be a linear graph that adheres to Beer's Lamberts Law. FTIR analysis should be used to determine whether silver nanoparticles and PEG 400 are compatible. Peaks in the silver nanoparticles-polymer PEG400 should not form or vanish since this would indicate that there hasn't been any chemical interaction between the two. It is necessary to make different oral dissolving films with variable composition amounts. By evaluating the effectiveness and nice texture of many formulations, the best formulation is chosen. Oral dissolving film with radix bupleuri silver nanoparticle is examined using SEM, and a TEM picture of the film is also examined. The ideal range for particle size is 10-110 nanometre.

In this study, numerous types of oral dissolving films are developed and optimised. PEG 400 is used to create a variety of oral dissolving film formulations. Utilising a variety of techniques, oral dissolving film evaluations are conducted. The produced oral dissolving film's physicochemical characteristics will be identified. The stability of the oral dissolving film should be assessed using a variety of characteristics, including surface pH, transparency, assay, disintegration time, dissolution time, and physical factors. To ascertain the antiviral activity of the formulation, several antiviral tests of the silver nanoparticles from Radix bupleuri that are included in the oral dissolving film should be conducted.

According to our outline research, the component of saikosaponin that is derived from *Radix bupleuri* possesses immunomodulatory, alleviating, and anti-diabetic effects. Our review revealed that saikosaponin has been used for a long time in a variety of conditions, including cancer, neuropathy, real health, pulmonary bunch disorders, immunomodulatory, etc. Saikosaponin has been tested for use in cases of COPD, asthma, influenza, rhinovirus, and other infections. It has a positive prognosis for recovery and lowers the death rate. We advise using Saikosaponin as a supplement to lessen lung inflammation and to prevent the post-COVID condition because COVID 19 has similar side effects to seasonal infections.
This study sets the door for creating a saikosaponin, a component of Radix bupleuri that will be isolated by green synthesis and added to an oral dissolving film that will have antiviral properties and greater efficacy against SARS Covid-19 Viral Strains.

Conflict of Interest:
The author declares no conflicts of interest.

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References

[1] Yuan B., Yang R., Ma Y., Zhou S., Zhang X., Liu Y. A systematic review of the active saikosaponins and extracts isolated from radix bupleuri and their applications.2016 Dec 12.
[2] Mengxun Zhang, Jiaqing Zhong, Yongai Xiong, Xun Song, Chenyang Li, Zhendan He, Development of Broad-Spectrum Antiviral Agents-Inspiration from Immunomodulatory Natural Products.
[3] Hong-Wei-Wang, Ming Liu, Tai-Di Zhong, Xiang-Ming Fang Saikosaponin-d attenuates ventilator-induced lung injury in rats.2015 September 15.
[4] Yan Y.-M., Shen X., Cao Y.-K., Zhang J.-J., Wang Y., Cheng Y.-X. Discovery of anti-2019-nCoV agents from Chinese patent drugs via docking screening. February 2020.
[5] Cheng P.-W., Ng L.-T., Chiang L.-C., Lin C.-C. Antiviral effects of saikosaponins on human coronavirus 229E in vitro 2006 Jun21
[6] Eshak I. Bahbah, Ahmed Negida, and Mohamed Salah Nabel Purposing Saikosaponins for the treatment of COVID-19.
[7] Abdelghany, T. M., Al-Rajhi, A. M., Al Abboud, M. A., Alawlaqi, M. M., Ganash Magdah, A., Helmy, E. A. and Mabrouk, A. S., Recent advances in green synthesis of silver nanoparticles and their applications: about future directions.2018.
[8] Bhattacharya, R. and Mukherjee, P., Biological properties of "naked" metal nanoparticles.2008.
[9] Furno, F., Morley, K. S., Wong, B., Sharp, B. L., Arnold, P. L., Howdle, S. M., Bayston, R., Brown, P. D., Winship, P. D. and Reid, H. J., Silver nanoparticles Bibliography 56 10. and polymeric medical devices: a new approach to prevention of infection.2004.
[10] Zhang, X. F., Liu, Z. G., Shen, W. and Gurunathan, S., Silver nanoparticles: synthesis, characterization, properties, applications, and therapeutic approaches.2016.
[11] Himani and garg rajeev oral dissolving films: a review, 2018.
[12] Ashish jain, harish c. Ahirwar, shivam tayal, pradeep k. Mohanty fast dissolving oral films: a tabular update, 2018.
[13] Nair SS, Padamanabhan R, Sreena K. Development and Evaluation of fast dissolving oral thin film containing prochlorperazine maleate.2016
[14] Patil JS, Deokar AB, Vilegave KV, Morani DO, Dhadde SB. Design, evaluation and characterization of rapidly dissolving oral strips of metoprolol succinate.2016.
[15] Bhupinder bhyan, sarita jangra, mandeep kaur, harmanpreet singh orally fast dissolving films: innovations in formulation and technology, 2011.
[16] Brniak W, Jachowicz R, Pelka Przemyslaw. The practical approach to the evaluation of methods used to determine the disintegration time of orally disintegrating tablets.2015.
[17] Kulkarni AS, Deokule HA, Exploration of different polymers for use in the formulation of oral fast dissolving strips.2010.
[18] Koland M, Charyulu N, Fast dissolving sublingual films of ondansetron hydrochloride: Effect of addivites on in vitro drug release and mucousal permeation.2010.
[19] Shimoda H, Taniguchi K, Preparation of fast dissolving oral thin film containing dexamethasone: A possible application to antiemesis during cancer chemotherapy.2009
[20] Andri Frediansyah, Firzan Nainu, Kuldeep Dhama, Mudatsir, and Harapan Remdesivir and its antiviral activity against COVID-19: A systematic review.2020.