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Research Article

Design, Development, And Evaluation Of Nanostructured Lipid Carriers (NLC S) For Efficient Nose-To-Brain Targeting In Alzheimer's Disease

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ABSTRACT

Picrorhiza kurroa Royle ex Benth is one of the most important medicinal plants, commonly used in traditional medicinal systems. The plant has several medicinal properties due to the presence of bio active components viz., Picroside I and Picroside II, cucurbitacins and phenolic components. These chemical compounds are found in the roots and rhizomes of this herb, and are used to cure various ailments such as liver problems, spleen disorder, fever and asthma. This perennial herb, known as "Kutaki" in various regional names, can grow up to 20 cm tall and has a branched stoloniferous root stock that perennates throughout the year. The study aims to develop and evaluate Nanostructured Lipid Carriers (NLCs) containing active plant constituents from Picrorhiza kurroa for efficient nose-to-brain targeting in Alzheimer's Disease (AD). The objective is to avoid side effects of oral therapy, provide fast onset of action, bypass blood brain barriers, increase bioavailability and biodistribution of drugs, and enhance the penetrating power of the formulation. The formulation will be evaluated for various parameters and optimized based on evaluation parameters. Nanoparticles, with a diameter of less than 200 nm and three layers, are biodegradable and non-toxic particles used in drug delivery. They can be filled with desired drugs, allowing lower drug doses and maintaining performance. The challenge in Alzheimer's management is to reach the gastrointestinal mucosa to target underlying inflammatory cells. Polymers like inulin and chitosan are used in NP formulations due to their biodegradability, biocompatibility, non-toxicity, aqueous solubility, and prebiotic effect on the gut microbial population. This study aimed to synthesize a novel biodegradable and biocompatible nanoparticulate system using ionic gelation technique and a model drug mesalazine for effective management of mental disorders. The Box Behnken factorial design design was used to study interactions and factors.

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The extract loaded Chitosan-CMI Nanoparticle drug delivery system was identified and its solubility determined using various solvents at room temperature.

INTRODUCTION

Picrorhiza kurroa Royle ex Benth is one of the most important medicinal plants, commonly used in traditional medicinal systems. The plant has several medicinal properties due to the presence of bio active components viz., Picroside I and Picroside II, cucurbitacins and phenolic components. These chemical compounds are found in the roots and rhizomes of this herb, and are used to cure various ailments such as liver problems, spleen disorder, fever and asthma. World annual demand of P. kurroa is 500 tons per year while production is 375 tons (1-3). It has become endangered in various regions due to indiscriminate exploitation for medicinal purposes. Immediate steps need to be taken for the conservation of this medicinal herb otherwise it will lead to extinction. Ayurveda, a part of Atharaveda in India, offers natural remedies for diseases. One of the herbal wealth is the "Kutaki" plant, Picrorhiza kurroa, found in the northwestern Himalayan region. This perennial herb, known as "Kutaki" in various regional names, can grow up to 20 cm tall and has a branched stoloniferous root stock that perennates throughout the year (4-6). The study aims to develop and evaluate Nanostructured Lipid Carriers (NLCs) containing active plant constituents from Picrorhiza kurroa for efficient nose-to-brain targeting in Alzheimer's Disease (AD). The objective is to avoid side effects of oral therapy, provide fast onset of action, bypass blood brain barriers, increase bioavailability and biodistribution of drugs, and enhance the penetrating power of the formulation. The formulation will be evaluated for various parameters and optimized based on evaluation parameters.

2. MATERIALS AND METHODS

2.1 Extraction of the Plant Materials

Roots of Picrorhiza kurroa were shade dried and grind coarsely and extracted using methanol through Cold Maceration technique.

2.2 Preparation of CS Nanoparticles

Chitosan-CMI nanoparticles were created by ionic gelation of chitosan's amino group with CMI's carboxyl group. Chitosan was dissolved in a lactic acid solution with 1.0 M NaOH, and CMI was dissolved in PBS at 0.5 mg/mL. 5-ASA was added to the CMI solution and completely dissolved. Chitosan-CMI nanoparticles were formed by mixing 100 mL of dissolved drug solution with 100 mL of chitosan solution at room temperature. The solution was centrifuged at 6,000 rpm for 20 minutes, and the precipitate was removed. The supernatant was filtered through a 1.0µm membrane filter to obtain the chitosan-CMI nanoparticle suspension. The nanoparticles were lyophilized for 48 hours to obtain powdered nanoparticles. The process involved a mixture of drug solution and chitosan solution, with the solution becoming slightly cloudy after 5 minutes of stirring (7-9).

2.3 Characterization of Chitosan-CMI Nanoparticulate System

The influence of a binary mixture of biopolymers & drug on physicochemical considerations including Particle size and size distribution, zeta potential, Poly dispersity index (PDI) & drug release was evaluated (10-12).

3. RESULTS AND DISCUSSION

3.1 Percentage Yield and Phytochemical Screening and Quantitative Estimation

The percentage yield of each extract along with the texture is mentioned in Table 1. All the extract showed presence of carbohydrates, proteins,



amino acids, alkaloids, saponins, sterols, tannins flavonoid content and total phenolic content and phenolic compounds flavonoids. The total mentioned in Table 2.

Table 1: Percentage Yield

Extract	Texture	Percentage Yield (%w/W)
Methanolic extract of roots of Picrorhiza kurroa (MEPK)	Greenish Blue	32.09

Table 2: Quantitative Estimation of Phytochemicals

Extracts	Total Flavonoid Content (mg quercetin equivalents/g of extract)	Total Phenolic Content (mg tannic acid equivalents/g of extract)
Methanolic extract of roots of Picrorhiza kurroa (MEPK)	41.48 ± 0.366	33.24 ± 0.411

3.2 Characterization of Chitosan-CMI Nanoparticulate System

The model's F-value is high at 77.75, indicating a significant impact on particle size. Factors A and B have the most significant impact on particle size, while factor C has little impact. The signal-to-noise ratio is accurate, with a positive 29.907 ratio indicating the model's usefulness in design. The

polyelectrolyte ratio influences the zeta potential/surface charge of developed nanoparticles, which is determined by their composition and dispersion medium. All formulations have a positive charge value, with OFMCI having the highest charge value of 36.58 and PDI 0.248 indicating good dispersion homogeneity and stability (Table 3).

Table 3: Zeta potential & Poly dispersity index (PDI) of all the formulation

Formulation Code	Zeta potential (mv± SD)	Poly dispersity index
F 1	35.46±1.3	0.232±0.02
F 2	35.18±1.0	0.248±0.04
F 3	28.36±1.5	0.355±0.08
F 4	22.36±2.0	0.355±0.10
F 5	25.98±3.4	0.245±0.12

3.3 In-vitro drug release profile of developed Chitosan-CMI nanoparticles

The study reveals that Extract-loaded nano-formulations showed minimal drug release at pH 7.4, followed by pH 1.2 and 6.8, but increased

exponentially in 7.4 pH buffer until 24 hours. The release profile of all formulations showed minimal drug release in acidic media due to the enzyme-sensitive polymer inulin and minimal hydration of the formulation. At higher pH, the chitosan present in the nanoparticle forms an interpenetrating

network, allowing for a sustained release pattern. The optimized nanoparticles exhibited a % CDR of 76.85% in 24 hours, indicating better-sustained release behavior compared to conventional tablets (Table 4; Figure 1).

Table 4: In-vitro drug release profile of developed Chitosan-CMI nanoparticles

Time (hrs.)	In-vitro drug release (%)				
	F1	F2	F3	F4	F5
0	0	0	0	0	0
1	7.03	7.12	8.02	10.59	12.59
2	12.15	13.56	15.62	20.55	23.68
3	19.27	19.22	21.12	26.89	30.12
4	25.26	27.56	29.26	33.25	36.59
5	34.37	35.98	37.59	41.58	45.68
6	41.97	45.26	46.89	49.58	51.26
8	48.44	49.26	50.15	53.59	59.54
10	56.70	57.21	59.46	63.58	65.26
12	61.24	63.26	64.59	69.59	70.14
24	68.11	69.75	70.18	73.89	79.59

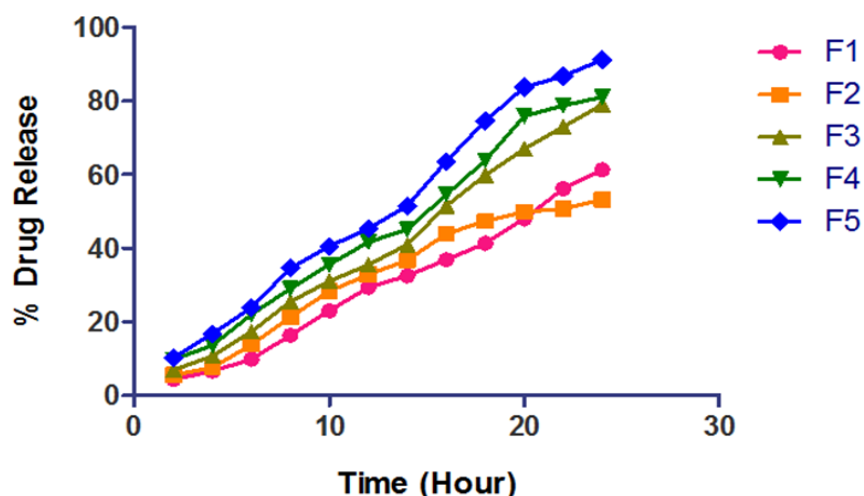


Figure 4: In-vitro drug release profile

3.4 Stability studies of optimized formulation (as per ICH guideline):

The encapsulation efficiency of optimized nanoparticle formulation (PN3) was found to

decrease sharply at 40°C after 10 days, while at 4°C or 25°C, it decreased slowly. The efficiency at 4°C decreased less than at 25°C and 40°C. Therefore, nanoparticle formulations should be stored at cold conditions. Stability of the drug was determined by keeping it within its physical, chemical, therapeutic, and toxicological specifications. Stability studies were conducted according to ICH Q1A (R2) guidelines, with the formulation wrapped in aluminum foil and kept in a stability chamber at 40° ± 2°C and 75% ± 5 RH for 1 month.

4. CONCLUSIONS

Nanoparticles, with a diameter of less than 200 nm and three layers, are biodegradable and non-toxic particles used in drug delivery. They can be filled with desired drugs, allowing lower drug doses and maintaining performance. The challenge in Alzheimer's management is to reach the gastrointestinal mucosa to target underlying inflammatory cells. Polymers like inulin and chitosan are used in NP formulations due to their biodegradability, biocompatibility, non-toxicity, aqueous solubility, and prebiotic effect on the gut microbial population. This study aimed to synthesize a novel biodegradable and biocompatible nanoparticulate system using ionic gelation technique and a model drug mesalazine for effective management of colon targeted disorders. The Box Behnken factorial design was used to study interactions and factors. The extract loaded Chitosan-CMI Nanoparticle drug delivery system was identified and its solubility determined using various solvents at room temperature.

5. Conflict of Interest

None.

REFERENCES

1. Singh DK, Hajra PK. Floristic diversity. In: G.S. Gujral, V. Sharma V. Changing perspective of biodiversity status in the Himalaya, British Council Division, Wildlife Youth Services. New Delhi: British High Commission Publication; 1996. p. 23-38.
2. Sharma PV. Classical Uses of Medicinal Plants. Varanasi: Chaukhambha Visvabharati; 1996. p. 69-70.
3. Fakim-Gurib A. Medicinal plants: traditions of yesterday and drugs of tomorrow. *Mol Aspect Med* 2006;1:93.
4. Simbo DJ. An ethnobotanical survey of medicinal plants in Babungu. Northwest Region: Cameroon. *J Ethnobiol Ethnomed* 2010;6:1-7.
5. Chintamunnee V, Mahomoodally MF. Herbal medicine commonly used against infectious diseases in the tropical island of Mauritius. *J Herb Med* 2012;2:113-25.
6. Ekor M. The growing use of herbal medicines: issues relating to adverse reactions and challenges in monitoring safety. *Front Pharmacol* 2014;4:177
7. Salvi VR, Pawar P. Nanostructured lipid carriers (NLC) system: A novel drug targeting carrier. *Journal of Drug Delivery Science and Technology*. 2019 Jun 1;51:255-67.
8. Müller RH, Radtke M, Wissing SA. Solid lipid nanoparticles (SLN) and nanostructured lipid carriers (NLC) in cosmetic and dermatological preparations. *Advanced drug delivery reviews*. 2002 Nov 1;54:S131-55.
9. Obeidat WM, Schwabe K, Müller RH, Keck CM. Preservation of nanostructured lipid carriers (NLC). *European Journal of Pharmaceutics and Biopharmaceutics*. 2010 Sep 1;76(1):56-67.
10. Müller RH, Alexiev U, Sinambela P, Keck CM. Nanostructured lipid carriers (NLC): the



second generation of solid lipid nanoparticles.
Percutaneous Penetration Enhancers Chemical
Methods in Penetration Enhancement:
Nanocarriers. 2016:161-85.

11. Müller RH, Petersen RD, Hommoss A, Pardeike J. Nanostructured lipid carriers (NLC) in cosmetic dermal products. *Advanced drug delivery reviews*. 2007 Jul 10;59(6):522-30.
12. Saupe A, Wissing SA, Lenk A, Schmidt C, Müller RH. Solid lipid nanoparticles (SLN) and nanostructured lipid carriers (NLC)—structural investigations on two different carrier systems. *Bio-medical materials and engineering*. 2005 Sep;15(5):393-402..

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