RESEARCH PAPER

Design And Optimization of Sulphated Locust Bean Gum Cationic Guar Gum Polyelectrolyte Complex Controlled Release Tablets

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ABSTRACT
The present study focused on the development and optimization of controlled release tablets based on polyelectrolyte complexes (PECs) of sulphated locust bean gum (SLBG) and cationic guar gum (CGG). Losartan potassium, a short half-life antihypertensive drug, was selected as the model candidate. PECs were prepared by ionic interaction of SLBG and CGG, blended with microcrystalline cellulose (MCC) as diluent, and compressed into tablets. A Box-Behnken design was employed to evaluate the effects of SLBG, CGG, and MCC on drug release at 2 hours and 10 hours. Statistical analysis demonstrated that both polymers significantly influenced release kinetics. An optimized ratio of 1.25:1 (SLBG:CGG) with MCC at 38.91 mg provided near stoichiometric charge balance with slight anionic excess, resulting in a hydrated and stable PEC network that enabled reproducible controlled release. The optimized tablets achieved 23.01% release at 2 hours and 88.11% release at 10 hours, matching the design criteria. Physicochemical characterization using FTIR, DSC confirmed drug stability without incompatibility. These findings establish SLBG-CGG PECs as a promising natural polymer platform for sustained oral delivery of losartan potassium, with potential applicability to other therapeutic agents.
Keywords: Polyelectrolyte complexes; Guar gum; Locust bean gum; Box-Behnken model; Losartan potassium.
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INTRODUCTION

Advancements in drug delivery systems have increasingly focused on optimizing excipient functionality to achieve precise control over drug release and therapeutic performance1. Among these, polyelectrolyte complexes (PECs) have emerged as a versatile platform, offering unique opportunities for oral drug delivery due to their ability to form stable, biocompatible networks through ionic interactions. PECs are generated when oppositely charged polymers interact electrostatically, producing complexes that can manifest as coacervates, nanoparticles, thin films, or matrix structures2.3. These assemblies are particularly attractive because they provide structural integrity and controlled drug release without the need for covalent crosslinking agents, thereby eliminating concerns associated with residual chemical crosslinkers and their potential cytotoxic effects3,4.

The release behavior of drugs from such systems is largely influenced by polymer composition, ionic density, and the degree of physical crosslinking, which together dictate network porosity and diffusional pathways4,5. Conventional chemical crosslinking agents, while effective in improving strength and stability, are often limited by safety concerns, harsh reaction requirements, and regulatory challenges6-14. In contrast, PEC-based physical crosslinking occurs under mild aqueous conditions, driven by counter-ion displacement, offering safer, simpler, and more eco-friendly fabrication. These systems also demonstrate dynamic responsiveness to physiological conditions such as pH and ionic strength, making them highly adaptable for oral controlled release applications2,3,10.

Although polyelectrolyte complexation is well studied for inherently ionic polymers, its extension to naturally neutral polysaccharides remains relatively underexplored. Chemical derivatization of non-ionic galactomannans such as locust bean gum (LBG) can introduce ionic groups, thereby enabling their participation in PEC formation. In this study, sulphated LBG was combined with cationic guar gum (CGG) to create novel ionic complexes aimed at achieving controlled drug delivery. Losartan potassium, a clinically established antihypertensive agent with a short elimination half-life (1–3 h), was selected as the model drug11. Its rapid clearance profile and frequent dosing requirement make it an appropriate candidate to evaluate the ability of PEC matrices to provide prolonged release. The present work thus emphasizes the design of a new excipient combination-sulphated LBG and CGG for controlled oral delivery of losartan potassium, highlighting their potential as safe and efficient release-retardant systems.

MATERIALS

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Losartan potassium was procured from Dharmtech Pharma and Consultants, Maharashtra. Cationic guar gum was purchased from Chimique India limited, Haryana, India, and locust bean gum from PY Chemical industries, Gujarat India. All other excipients and reagents were of analytical grade and were purchased from Sigma-Aldrich, Bangalore, India.

METHODS

3.1. Response surface methodology by Box-Behnken design

Response Surface Methodology using Box-Behnken model was applied to optimize the formulation and establish the design space for the controlled release losartan potassium controlled release tablets. The optimization was performed using JMP® software (Version 18.0.1., JMP Statistical Discovery LLC, 2024), with SLBG, CGG and MCC as independent factors at levels illustrated in Table 1, with percentage cumulative drug release as response. The design resulted in 15 formulations in order to establish the design space.

Table 1: Optimization levels of factors in Box-Behnken design

Factors chosen	Levels of optimization		
	-1	0	+1
SLBG (X_1, mg)	40	60	80
CGG (X_2, mg)	40	60	80
MCC (X_3, mg))	30	40	50

3.2. Preparation of PEC controlled release tablets of losartan potassium

For the preparation of the polyelectrolyte complex (PEC) based tablets, predetermined quantities of sulphated locust bean gum (SLBG) and cationic guar gum (CGG) were weighed accurately and combined in specific ratios for each experimental run (Table 2). Both polymers were dispersed in purified water at a 1:10 w/v ratio and subjected to continuous stirring for 1 hour to ensure uniform hydration and initial interaction of the oppositely charged chains (wet massing). The hydrated dispersions were then allowed to stand undisturbed for 4-6 hours, and in some cases overnight at ambient conditions, to facilitate electrostatic complexation and network formation12. The resulting wet mass was dried in a hot air oven at 50-60 °C until a constant weight was achieved, thereby ensuring complete removal of moisture. The dried complexes were grind to get fine particles and passed through a #40 mesh sieve to obtain free-flowing particles suitable for compression.

For drug incorporation, losartan potassium equivalent to 50 mg per tablet was blended with the PEC particles along with MCC as a diluent to improve compressibility. Finally, magnesium stearate and talc were incorporated at a fixed level of 5 mg each per formulation, corresponding to 2-4% w/w, which falls within Pharmacopeial recommendations for lubricants and glidants. The final blend was evaluated for flow properties prior to compression into tablets.

Table 2: Box-Behnken design of SLBG, CGG PEC controlled release tablets

Run	PEC (mg)	MCC (mg)	Drug (mg)	Magnesium. stearate (mg)	Talc (mg)	Final Tablet Weight (mg)
L1G1M2	80	40	50	2.5	2.5	175
L1G2M1	100	30	50	2.5	2.5	185
L1G2M3	100	50	50	2.5	2.5	205
L1G3M2	120	40	50	2.5	2.5	215
L2G1M1	100	30	50	2.5	2.5	185
L2G1M3	100	50	50	2.5	2.5	205
L2G2M2	120	40	50	2.5	2.5	215
L2G2M2	120	40	50	2.5	2.5	215
L2G2M2	120	40	50	2.5	2.5	215
L2G3M1	140	30	50	2.5	2.5	225
L2G3M3	140	50	50	2.5	2.5	245
L3G1M2	120	40	50	2.5	2.5	215
L3G2M1	140	30	50	2.5	2.5	225
L3G2M3	140	50	50	2.5	2.5	245
L3G3M2	160	40	50	2.5	2.5	255

EVALUATION OF PEC CONTROLLED RELEASE TABLETS

4.1. Tablet micrometric and compression characterization

The powder blend was assesses for micrometric properties employing standard methods proposed, Carr's index and Hausners's ratio was calculated form the measured densities13. Angle of repose was determined through fixed funnel method14. The powder blend was compressed to form tablets using Mini Tablet Press Semiautomatic machine. The prepared tablets were

evaluated for various physicochemical and performance parameters. General appearance was assessed visually, considering shape, surface texture, and the absence of cracks or visible defects. Tablet thickness was determined for five randomly selected units from each batch using a Vernier caliper, while hardness was measured using a Monsanto hardness tester15. Weight variation was assessed on 20 tablets individually, and the mean weight and percentage deviation were calculated in accordance with Indian Pharmacopoeial limits16. Friability was evaluated using a Roche friabilator operated at 25 rpm for 100 revolutions17. For drug content uniformity, 10 tablets were powdered, and an amount equivalent to 50 mg of losartan potassium was accurately weighed and dissolved in 0.1 N HCl. The solution was filtered, and the drug content was quantified by UV-visible spectrophotometry at 234 nm against a suitable blank18.

4.2. In vitro drug release studies

Dissolution testing was performed using a USP type II (paddle) apparatus. Each test employed 900 ml of dissolution medium maintained at 37 ± 0.5 °C and agitated at 50 rpm. Initially, drug release was studied in 0.1 N HCl for 2 hours, simulating gastric conditions, followed by phosphate buffer (pH 6.8) for the subsequent 10 hours to mimic intestinal fluid. Aliquots were withdrawn at predetermined intervals, filtered, and analyzed spectrophotometrically for losartan potassium concentration. The cumulative release profiles were fitted to kinetic models, including zero-order, first-order, Higuchi, Hixson-Crowell, and Korsmeyer-Peppas equations. The most appropriate release mechanism for each formulation was identified based on the highest coefficient of determination (R^2)19,20.

4.3. Zeta potential

The surface charge of the polyelectrolyte complexes (PECs) was determined by zeta potential analysis. A dilute suspension of the PEC powder at optimized ratio was prepared by dispersing a known amount in double-distilled water, followed by ultrasonication to ensure uniform dispersion and minimize aggregation21. The sample was analyzed using a dynamic light scattering instrument equipped with electrophoretic mobility detection.

4.4. FTIR Spectroscopy

FTIR spectroscopy was employed to evaluate potential interactions between the drug and excipients. Pure drug, polymers, and PEC optimized tablet formulation were individually blended with potassium bromide (1% w/w) and compressed into transparent pellets using a mini pellet press. The spectra were recorded in the range of 4000–500 cm^{-1} using a Bruker FTIR spectrometer22.

4.5. Differential Scanning Calorimetry

Thermal properties of losartan potassium, and tablet formulations were studied using a METTLER DSC system. Samples (5–10 mg) were sealed in flat aluminum pans and analyzed under a nitrogen purge to prevent oxidative degradation. The heating program was set from 25 °C to 350 °C at a controlled rate of 10 °C/min. Thermograms were evaluated for drug melting point, and possible shifts or disappearance of endothermic peaks23.

RESULTS AND DISCUSSION

5.1. Preparation of PEC controlled release tablets of losartan potassium

The PECs formation depends on the charge distribution over the polymers, hence both the polymers SLBG and CGG were selected as factors for optimization process. Unlike, SLBG and CGG, MCC, the commonly used diluent was used as another factor. MCC role in maintenance and depletion of polymer integrity is a well-established fact24. Hence to avoid differences in release characteristics after establishment of the best polymer ratio for formation of PECs.

5.2. Evaluation of PEC controlled release tablets

5.2.1. Tablet micrometric and compression characterization

The powder blend of losartan potassium and excipients were uniformly mixed and evaluated for micrometric properties (Table 3). Powder blends of L1G1M2-L3G3M2 showed an angle of repose of less than 23.9º. The Hausner's ratio calculated was less than 1.12, with carr's index in the range of 8.87-13.81. These flow properties indicate that powder blend showed good flow properties, which can be attributed to the fine grind particles of the prepared PEC complex after precipitation. The variation in percentage composition of the excipients has not shown much variation or influence on the flow properties of the powder blend might be due to the small particle size of all the excipients used.

Table 3: Micrometric properties of losartan potassium controlled release PEC tablets

Code	Hausner's ratio	Angle of repose	Carr's index
L1G1M2	1.10	22.3±0.16	10.78
L1G2M1	1.11	21.7±0.23	12.82
L1G2M1	1.12	22.8±0.10	13.81
L1G3M2	1.08	21.4±0.08	8.89
L2G1M1	1.10	22.4±0.22	10.96
L2G1M3	1.11	23.3±0.26	11.66
L2G2M1	1.11	23.3±0.30	11.80
L2G2M3	1.08	20.1±0.15	8.87
L2G3M1	1.11	23.5±0.32	11.64

L2G2M2	1.11	22.9±0.78	11.66
L2G3M3	1.11	23.6±0.44	11.64
L3G1M2	1.08	21.8±0.12	8.90
L3G2M1	1.12	23.9±0.37	13.76
L3G2M3	1.11	23.5±0.48	11.64
L3G3M2	1.10	22.6±0.28	10.77

The tablet hardness was maintained in an average of 5 kg/cm2 (Table 4). As expressed in the formulation table, the total weights of the tablets were not corrected to constant weight in order to understand the influence of all the three factors accurately. Hence the total weight varied between 175 mg to 255 mg. However, in the uniformity of the weight test the mean±s.d values remained within range i.e., ±7.5% w/w for below 250 mg tablets and ±5% w/w for above 250 mg tablets. The thickness also varied based on the total weight, which ranged between the 2.28-2.92 mm. L1G1M2-L3G3M2 showed friability values less than 1% and maintained an average drug content of 99% with less standard deviation, falling under the standard limits.

Table 4: Tablet characteristics of losartan potassium controlled release PEC tablets

Code	Thickness[a] (mm)	Hardness[a] (kg/cm^2)	Uniformity of weight[b] (mg)	Friability[c] (%)	Drug content[d] (%)
L1G1M2	**2.27±0.01**	**5.1±0.04**	**175±1.44**	**0.57±0.03**	**99.44±0.19**
L1G2M1	**2.28±0.02**	**5.1±0.03**	**185±1.13**	**0.59±0.01**	**99.69±0.94**
L1G2M1	**2.28±0.02**	**5.4±0.05**	**205±1.05**	**0.61±0.01**	**99.40±1.03**
L1G3M2	**2.53±0.04**	**5.0±0.07**	**215±1.11**	**0.52±0.04**	**99.56±0.89**
L2G1M1	**2.28±0.03**	**5.4±0.03**	**185±1.40**	**0.63±0.02**	**99.41±0.80**
L2G1M3	**2.50±0.05**	**5.6±0.03**	**205±1.09**	**0.58±0.01**	**99.57±0.61**
L2G2M1	**2.50±0.03**	**5.3±0.06**	**215±1.24**	**0.62±0.03**	**99.75±0.42**
L2G2M3	**2.60±0.08**	**5.5±0.04**	**215±1.32**	**0.61±0.01**	**99.53±0.21**
L2G3M1	**2.61±0.02**	**5.7±0.02**	**215±1.13**	**0.59±0.01**	**99.49±0.72**
L2G2M2	**2.53±0.08**	**5.5±0.04**	**225±1.03**	**0.59±0.02**	**99.33±0.86**
L2G3M3	**2.80±0.01**	**5.1±0.04**	**245±1.23**	**0.52±0.04**	**99.90±0.35**
L3G1M2	**2.53±0.02**	**5.1±0.03**	**215±1.05**	**0.58±0.01**	**99.82±0.77**
L3G2M1	**2.61±0.04**	**5.0±0.07**	**225±1.19**	**0.52±0.04**	**99.85±0.55**
L3G2M3	**2.81±0.03**	**5.3±0.06**	**245±1.28**	**0.62±0.03**	**99.92±0.51**
L3G3M2	**2.92±0.02**	**5.4±0.05**	**255±1.21**	**0.59±0.02**	**99.32±0.64**

a: mean±s.d, n=5; b: mean±% deviation, n=20; c: tablets equivalent 6.5 g; d: mean±s.d., n=3

5.2.2. In vitro drug release studies

For a controlled release formulation, maintaining appropriate drug concentration throughout the release period is the primary objective, at the same time reaching the minimum therapeutic level without much lag is also equally important, hence in the evaluation of independent factors on the in vitro losartan potassium release % cumulative drug release at 2 hours and 10 hours were selected as responses, as no official tolerance limits for dissolution were suggested for losartan potassium. The objective release range chosen for the optimization was 20-25% at 2 hours and 85-90% for 10 hours and the cumulative percentage drug release of L1G1M2-L3G3M2 (Table 5) were subjected to analysis. The fit statistics imply insignificant lack of fit with a p >0.05, and actual by predicted plot with a R2 value of 0.9958 and p<0.0001 for data at 2 hours. Drug release data at 10 hours also showed good fit statistics with lack of fit p value of 0.837 and actual by predicted plot with R2 value of 0.9976 and p<0.0001. A perfect fit statistics indicate the reliability of the conclusions made from the model.

The cumulative percentage drug release at 2 hours (Table 6) was significantly influenced by all three formulation variables: sulfated locust bean gum (SLBG), cationic guar gum (CGG), and microcrystalline cellulose (MCC). The individual effects of each factor were evident, with SLBG and CGG primarily modulating the swelling and matrix integrity, thereby governing early drug diffusion, while MCC contributed by modulating porosity and wettability of the compact. However, the interaction term between SLBG and CGG was the only polymer-polymer interaction found significant, suggesting that their ionic complexation and synergistic gelling capacity exerted greater control over the initial release than MCC related interactions, which remained statistically insignificant. The quadratic term of SLBG (SLBG^2) also showed significance at this stage, indicating that nonlinear effects of polymer concentration strongly impacted the extent of drug release in the initial hours, most likely due to variations in gel layer thickness and initial hydration behavior.

Table 6: Parameter estimates of the factors based on drug release at 2 hours

Term	Estimate	Std Error	Prob>|t|
Intercept	19.18	0.362517	<.0.0001*
SLBG(40,80)	-4.53	0.221995	<.0.0001*
CGG(40,80)	-5.93875	0.221995	<.0.0001*

MCC(30,50)	0.99875	0.221995	0.0064*
SLBG*CGG	-1.0975	0.313949	0.0174*
SLBG*MCC	-0.3125	0.313949	0.3652
CGG*MCC	-0.165	0.313949	0.6217
SLBG*SLBG	1.6775	0.326768	0.0037*
CGG*CGG	0.695	0.326768	0.0867
MCC*MCC	0.06	0.326768	0.8615

At 10 hours (Table 7), the release behavior was again significantly governed by SLBG, CGG, and MCC, along with the interaction between SLBG and CGG. This indicates that long term release is dictated by a balance of polymer concentration, their polyelectrolyte complexation, and filler contribution to matrix structure. Both SLBG and CGG act as release retardants through network formation, while MCC aids sustained diffusion by maintaining tablet integrity and hydration balance. The quadratic contribution of CGG (CGG^2) was significant at this time point, suggesting that higher concentrations of CGG may impart a nonlinear retardation effect on prolonged release, possibly due to formation of denser gel matrices restricting diffusion pathways. Overall, the results demonstrate that while all three components contribute to both early and late release kinetics, the interplay between SLBG and CGG is the dominant factor governing the drug release mechanism across the time course. MCC primarily influenced drug release by enhancing tablet porosity and wettability, thereby facilitating medium penetration and initial drug diffusion. Its contribution was supportive rather than dominant, ensuring matrix integrity and uniform hydration without significantly altering polymer-polymer interactions.

Table 7: Parameter estimates of the factors based on drug release at 10 hours

Term	Estimate	Std Error	Prob>|t|
Intercept	84.013333	0.344325	<0.0001*
SLBG(40,80)	-6.11375	0.210855	<.0.0001*
CGG(40,80)	-7.175	0.210855	<.0.0001*
MCC(30,50)	2.04625	0.210855	0.0002*
SLBG*CGG	-0.805	0.298194	0.0428*
SLBG*MCC	0.2775	0.298194	0.3948
CGG*MCC	0.475	0.298194	0.1721
SLBG*SLBG	0.4770833	0.31037	0.1849
CGG*CGG	0.8445833	0.31037	0.0417*
MCC*MCC	-0.297917	0.31037	0.3812

Based on the parameter estimates, SLBG and CGG caused a decrease in the drug release with an increase in concentration individually and also in combination. But MCC showed a reversal effect, it promoted the drug release percentage with an increase in the concentration. This effect was more pronounced after dissolution for 10 hours compared to the 2 hours. Similarly the polymer retardation effect also increased with better hydration and swelling, which is evident from the magnitude of the parameter estimates. Based on the response factor relationships, a prediction profile suggested an optimized formula to achieve the objective release (Figure 1).

The optimization output recommends a composition of 57.7642 mg (58) sulfated SLBG, 46.1201 (46) mg CGG, and 38.9134(39) mg MCC, corresponding to an SLBG:CGG mass ratio of nearly 1.25:1. At this stoichiometry, the polyelectrolyte complex formed between the anionic sulfate groups on SLBG and the cationic sites on CGG achieves near optimal charge compensation without over neutralization. Taken together, the recommended formulation balances PEC density and hydration to deliver predictable early phase moderation and late phase completeness of release.

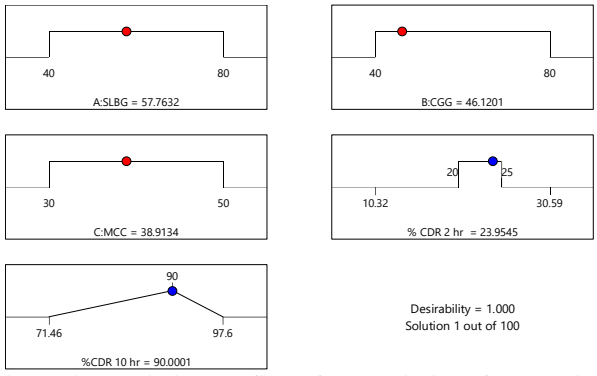

Figure 1: Prediction profiler of the optimized formulation

The formula was prepared for practical implementation and in vitro drug release were performed to establish the reliability of the suggestions. During the preparation of the controlled release losartan potassium PEC tablets with a constant weight the MCC (2.5mg) is utilized as diluent. From the percentage drug release it is clear that the optimum formula can be practically executed attaining the objective release profile as represented in the Figure 2. Using a statistical optimization design (e.g., Box-Behnken) to determine the PEC polymer ratio is superior to the conventional trial and error stoichiometry approach because it quantifies the relationships between polymer amounts, processing variables, and functional responses (e.g., % release at 2 hours and 10 hours). Optimization allows exploration of interactions among factors, reveals practical operating windows (e.g., slight anionic excess that maximizes desirable hydration without over-softening), and minimizes material use by identifying an engineered optimum instead of relying on single-point empirical guesses. This systematic strategy therefore yields a formulation that is reproducible, tunable, and supported by statistical evidence essential for robust scale up and regulatory documentation.

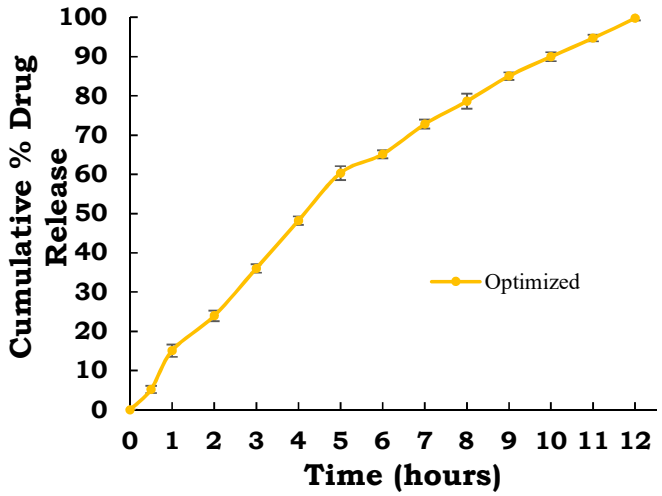

Figure 2: In vitro drug release profile of losartan potassium controlled release PEC tablets

CONCLUSION:

This investigation successfully demonstrated that sulphated locust bean gum and cationic guar gum can be engineered into stable polyelectrolyte complexes for controlled release drug delivery. The Box Behnken optimization revealed that polymer ratio and crosslinking interactions primarily govern drug release, while MCC acted as a diluent without significant mechanistic influence. Importantly, a slight excess of SLBG ensured hydrated networks that balanced sustained release with adequate swelling. The optimized formulation achieved predictable drug release over 12 hours, highlighting the advantage of PEC based design over conventional polymer blends. Thus, SLBG-CGG PECs represent an efficient, biocompatible, and scalable platform for developing next generation gastroretentive and controlled release dosage forms.

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8. Conflict of interest:

Authors declare no conflict of interest.

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