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Formulation and Characterization of Daridorexant Floating Raft-Forming In Situ Gel for Gastroretentive Drug Delivery

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Abstract: This study developed and evaluated a daridorexant floating raft-forming in situ gel for prolonged gastric retention and controlled nighttime drug delivery. Six formulations, DRG1–DRG6, were prepared using sodium alginate, calcium carbonate, sodium bicarbonate and Tween 80. The formulations were assessed for appearance, pH, viscosity, gelation time, raft strength, floating lag time, total floating duration, drug content, in vitro release, release kinetics and accelerated stability. Increasing sodium alginate and calcium carbonate concentrations improved gelation, raft strength and buoyancy while slowing drug release. DRG4 showed the most balanced performance, with pH 7.26 ± 0.03, viscosity 428.2 ± 19.4 mPa·s, gelation time 31 ± 2 s, raft strength 8.12 ± 0.48 g, floating lag time 28 ± 2 s, drug content 99.18 ± 1.16% and 94.18% release at 12 h. Release followed the Korsmeyer-Peppas model, indicating anomalous transport. DRG4 remained stable for three months under accelerated conditions without meaningful changes in performance parameters.

Keywords: Daridorexant, raft-forming in situ gel, gastroretentive delivery, sodium alginate, controlled release, insomnia, buoyancy.

INTRODUCTION

Insomnia is a common sleep disorder characterized by difficulty initiating sleep, maintaining sleep, or obtaining restorative sleep. Pharmacological therapy is used when symptoms are persistent and clinically

relevant, but dosage-form design remains important because drug release, gastrointestinal residence, and administration time can influence pharmaceutical performance [1–4].

Daridorexant is a dual orexin receptor antagonist developed for insomnia. It reduces wake-promoting orexin signalling and is administered orally. Although the drug is already available as an oral dosage form, a gastroretentive formulation can be investigated as a formulation strategy to prolong gastric residence and provide controlled nighttime release rather than as proof of superior clinical efficacy [5–8].

Gastroretentive drug-delivery systems are intended to remain in the stomach longer than conventional dosage forms. Floating and raft-forming systems achieve this by generating or entrapping gas within a hydrated polymeric matrix, thereby reducing apparent density and prolonging buoyancy. Their performance depends on polymer concentration, gas generation, gel strength, gastric fluid availability, and the ability of the matrix to remain sufficiently coherent during drug release [9–12].

Sodium alginate is widely used in raft-forming formulations because it rapidly hydrates and forms gels in the presence of calcium ions. Calcium carbonate can provide calcium for gel formation and also contribute to gas generation in acidic medium, while sodium bicarbonate supports buoyancy. The balance among viscosity, gelation time, raft strength, floating lag, and drug release is therefore critical; excessive polymer may improve raft strength but reduce pourability and retard drug release [13–16].

Previous studies on alginate-based floating and raft-forming systems support the feasibility of this approach for gastroretentive delivery [17–20]. Accordingly, the present study formulated six daridorexant raft-forming in situ gels and evaluated their physicochemical properties, buoyancy, raft characteristics, drug content, in vitro release, and short-term accelerated stability.

MATERIALS AND METHODS

Chemicals

Deridorexant was obtained from Gift sample from Unichem laboratories Ltd., Mumbai. Sodium alginate was obtained from Global Exports Private Ltd., Mumbai. Tween 80 was obtained from Global Exports Private Ltd., Mumbai. Sodium bicarbonate was obtained from S.D. FineChem Limited, Mumbai. Calcium carbonate was obtained from S.D. FineChem Limited, Mumbai.

Preformulation and analytical studies

Daridorexant was subjected to routine preformulation testing, UV analysis at 271 nm, and compatibility assessment with the selected polymer. The calibration relationship was used for quantitative estimation.

Formulation design

Six formulations, DRG1–DRG6, were prepared with a constant daridorexant dose while sodium alginate and calcium carbonate concentrations were varied. Sodium bicarbonate and Tween 80 were maintained according to the formulation matrix.

Table 1: Formulation composition of daridorexant raft-forming in situ gels

Formulation	DRX	Sodium alginate	Calcium carbonate	Sodium bicarbonate	Tween 80	Purified water q.s.
DRG1	25	1.00	0.50	0.50	0.10	10 mL
DRG2	25	1.00	0.75	0.50	0.10	10 mL
DRG3	25	1.25	0.50	0.50	0.10	10 mL
DRG4	25	1.25	0.75	0.50	0.10	10 mL
DRG5	25	1.50	0.50	0.50	0.10	10 mL
DRG6	25	1.50	0.75	0.50	0.10	10 mL

Note: All ingredients are in mg.

Preparation method

Sodium alginate was gradually dispersed in purified water and allowed to hydrate. Daridorexant was triturated with Tween 80 and a small quantity of water and incorporated into the hydrated alginate. Calcium carbonate and sodium bicarbonate were then dispersed under gentle stirring, and the final volume was adjusted with purified water. The same procedure was used for all six batches, with only the specified formulation variables changed.

FTIR compatibility study

FTIR spectra of pure daridorexant, sodium alginate, and the optimized formulation were recorded over 4000–400 cm^{-1} and compared for retention, shifting, broadening, appearance, or disappearance of characteristic bands.

Evaluation

The formulations were evaluated for appearance, pH, viscosity, gelation time, raft strength, floating lag time, total floating duration, and drug content. These parameters were used to assess pourability before administration and formation of a coherent floating raft after contact with acidic medium.

In vitro drug release

In vitro release was evaluated in 0.1 N HCl at pH 1.2 under the paddle conditions reported in the thesis, with sampling continued for 12 h and daridorexant quantified spectrophotometrically.

Stability study

The optimized formulation was stored at 40 ± 2°C/75 ± 5% RH for three months and reassessed for the principal physical and release characteristics.

RESULTS AND DISCUSSION

Drug-excipient compatibility

The major characteristic bands of daridorexant were retained in the optimized formulation with limited shifts and spectral overlap. No unexpected new major band was reported, supporting the absence of a major chemical incompatibility with sodium alginate.

Table 2: Comparative FTIR peak assignments of daridorexant, sodium alginate, and optimized formulation

Functional group	Pure Deridorexant (cm^{-1})	Sodium alginate (cm^{-1})	Optimized formulation (cm^{-1})
O–H / N–H stretching region	3295	3420	3392
Aliphatic C–H stretching	2928	2927	2928
Carbonyl stretching region	1712	–	1710
Carbonyl or aromatic associated region	1654, 1602	1603	1622
CH bending / carboxylate region	1496	1415	1414
C–O / C–N fingerprint region	1258, 1170, 1108	1095, 1030	1250, 1092, 1032
Aromatic out-of-plane region	760	–	760

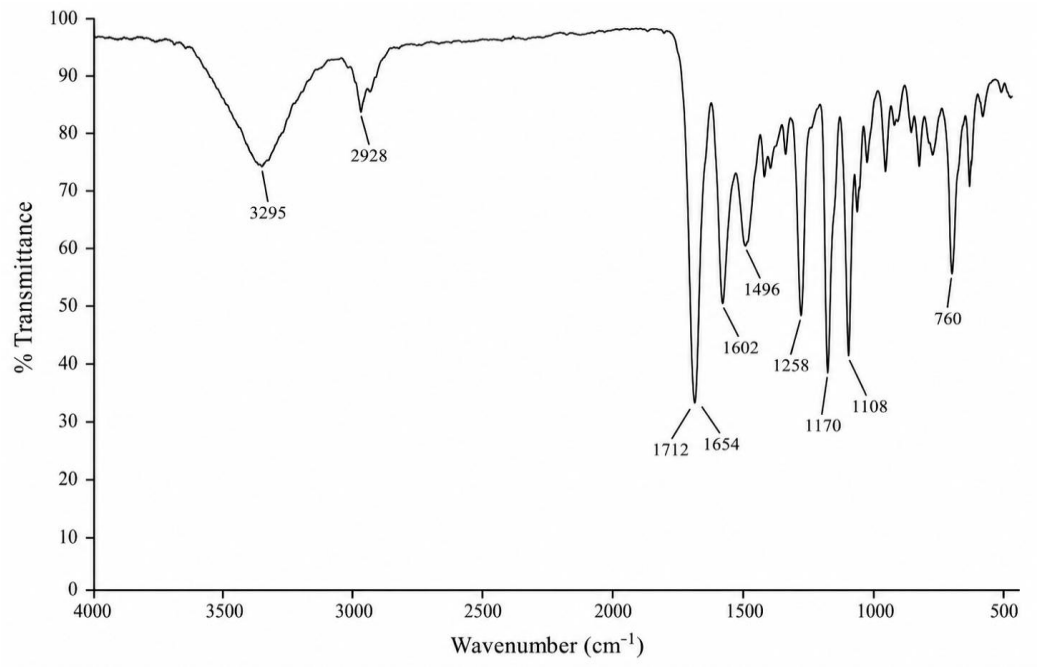

Fig 1: FTIR spectrum of pure daridorexant.

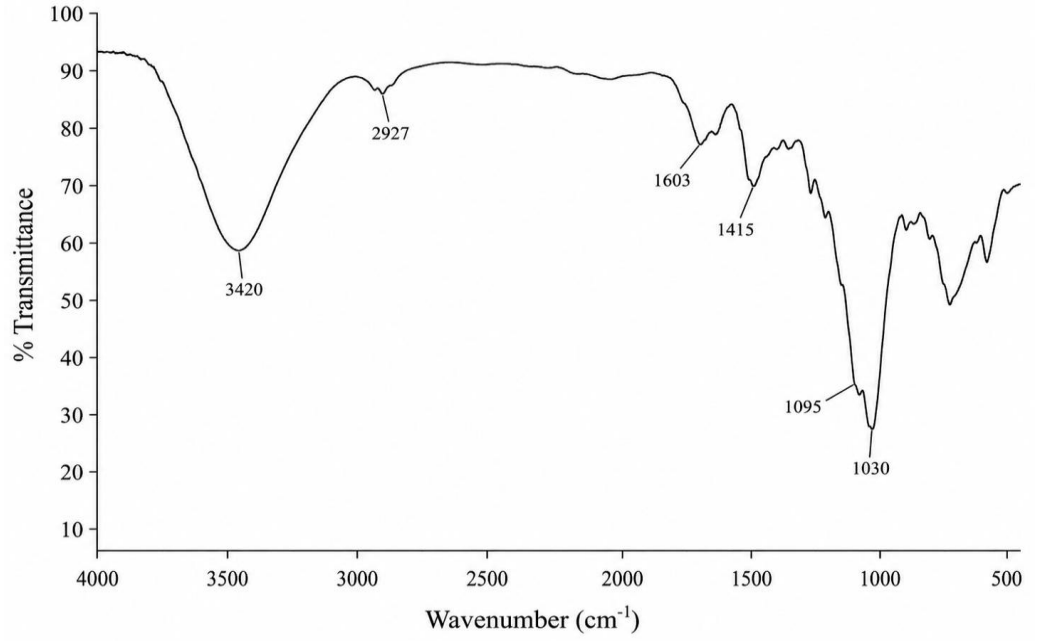

Fig 2: FTIR spectrum of sodium alginate.

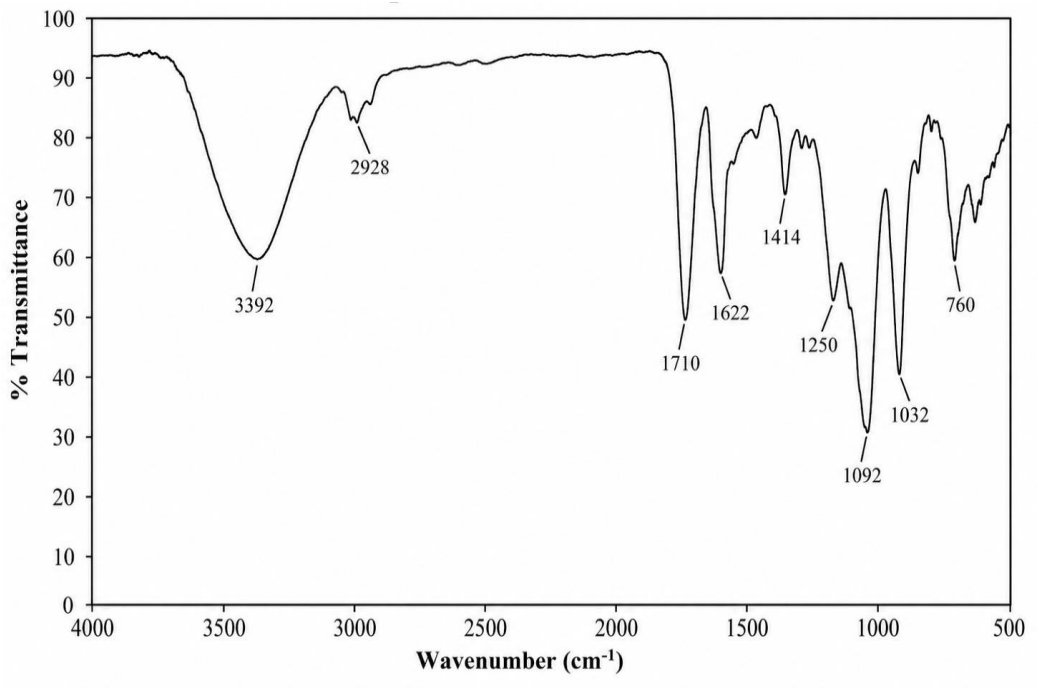

Fig 3: FTIR spectrum of the optimized formulation.

Physicochemical and raft-forming properties

All six batches were uniform without visible phase separation. Increasing sodium alginate and calcium carbonate increased viscosity and raft strength while shortening gelation and floating lag time. Drug content remained within the reported acceptable range. DRG4 provided a balanced combination of pourability, gelation, raft strength, and buoyancy.

Table 3: Appearance, pH, viscosity, gelation time, and raft strength

Batch	Appearance	pH	Viscosity (mPa·s)	Gelation time (s)	Raft strength (g)
DRG1	Uniform whitish dispersion	7.18 ± 0.04	284.6 ± 12.8	52 ± 3	4.86 ± 0.31
DRG2	Uniform whitish dispersion	7.21 ± 0.05	296.4 ± 14.2	44 ± 2	5.72 ± 0.36
DRG3	Smooth viscous dispersion	7.24 ± 0.04	412.8 ± 18.6	39 ± 2	6.84 ± 0.42
DRG4	Smooth viscous dispersion	7.26 ± 0.03	428.2 ± 19.4	31 ± 2	8.12 ± 0.48
DRG5	Thick uniform dispersion	7.29 ± 0.05	562.6 ± 24.8	34 ± 2	8.46 ± 0.51
DRG6	Thick uniform dispersion	7.31 ± 0.04	578.4 ± 26.2	26 ± 2	9.38 ± 0.57

Table 4: Floating behaviour and drug content

Batch	Floating lag time (s)	Total floating time (h)	Drug content (%)
DRG1	58 ± 4	7.2 ± 0.4	96.84 ± 1.42
DRG2	46 ± 3	8.6 ± 0.5	97.26 ± 1.36
DRG3	39 ± 3	9.8 ± 0.6	98.12 ± 1.28
DRG4	28 ± 2	11.7 ± 0.5	99.18 ± 1.16
DRG5	34 ± 3	10.9 ± 0.6	98.46 ± 1.31

DRG6	24 ± 2	>12	98.72 ± 1.24

In vitro drug release and optimized formulation

Drug release decreased as the raft-forming matrix became stronger. Lower-polymer batches released daridorexant more rapidly, whereas higher-polymer formulations produced greater release retardation. DRG4 showed pH 7.26 ± 0.03, viscosity 428.2 ± 19.4 mPa·s, gelation time 31 ± 2 s, raft strength 8.12 ± 0.48 g, floating lag time 28 ± 2 s, drug content 99.18 ± 1.16%, and 94.18% release at 12 h. It was therefore selected as the optimized batch.

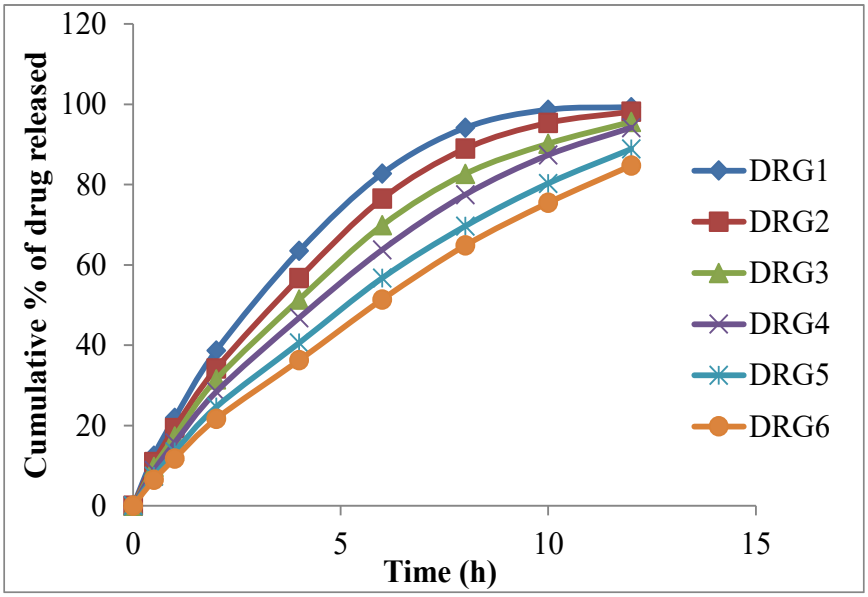

Fig 4: In vitro drug-release profiles of daridorexant raft-gel formulations.

Stability study

DRG4 remained physically stable during three months of accelerated storage, with no visible separation or precipitation and only minor changes in pH, viscosity, drug content, and release.

CONCLUSION

Daridorexant floating raft-forming in situ gels were successfully prepared using sodium alginate with calcium carbonate and sodium bicarbonate. Polymer and calcium levels influenced viscosity, gelation, raft strength, buoyancy, and release. DRG4 showed the most balanced overall performance and released 94.18% of daridorexant over 12 h while remaining pourable before gelation. The formulation also retained acceptable characteristics during the three-month accelerated study.

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