FORMULATION AND EVALUATION OF ORODISPERSIBLE TABLETS OF AMITRIPTYLINE HYDROCHLORIDE BY DIRECT COMPRESSION METHOD

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Abstract

The present study aimed to formulate and evaluate orodispersible tablets (ODTs) of Amitriptyline Hydrochloride using the direct compression method. Nine formulations (F1–F9) were prepared using varying concentrations of superdisintegrants and commonly used excipients such as mannitol, microcrystalline cellulose, and lactose monohydrate. The prepared tablets were evaluated for pre-compression and post-compression parameters including angle of repose, bulk density, Carr's index, hardness, friability, weight variation, wetting time, dispersion time, drug content, and in-vitro dissolution studies. FTIR compatibility studies confirmed the absence of drug–excipient interactions. Stability studies demonstrated the stability of optimized formulation under accelerated conditions. Among all batches, formulation F8 showed rapid disintegration and maximum drug release within 15 minutes. The study concludes that direct compression is a suitable method for preparing stable and patient-compliant ODTs of Amitriptyline Hydrochloride.

Keywords
Amitriptyline Hydrochloride, Orodispersible Tablets, Direct Compression, Superdisintegrants, Dissolution, FTIR, Stability Study

Introduction

Oral drug delivery remains the most preferred and widely accepted route of administration due to its convenience, cost effectiveness, patient compliance, and ease of manufacturing. However, conventional oral tablets are often associated with swallowing difficulties, particularly in pediatric, geriatric, bedridden, and psychiatric patients. Dysphagia, or difficulty in swallowing, affects a significant portion of the population and may lead to poor patient compliance, improper dosing, and reduced therapeutic efficacy. To overcome these limitations, the pharmaceutical industry has focused on the development of patient-friendly novel dosage forms such as Orodispersible Tablets (ODTs). Orodispersible tablets are solid unit dosage forms that disintegrate or dissolve rapidly in the saliva within a few seconds without the need for water. According to the United States Food and Drug Administration (USFDA), ODTs are tablets that disintegrate rapidly, usually within 30 seconds, when placed upon the tongue. These formulations provide several advantages including rapid onset of action, improved bioavailability, ease of administration, accurate dosing, enhanced patient compliance, and improved stability compared to liquid dosage forms. ODTs are particularly beneficial for patients suffering from neurological disorders, motion sickness, mental illness, and conditions associated with nausea or difficulty in swallowing. Amitriptyline Hydrochloride is a tricyclic antidepressant widely prescribed for the treatment of major depressive disorders, anxiety disorders, neuropathic pain, migraine prophylaxis, and insomnia. The drug acts primarily by inhibiting the reuptake of norepinephrine and serotonin at neuronal synapses, thereby enhancing neurotransmission in the central nervous system. Despite its therapeutic effectiveness, Amitriptyline Hydrochloride exhibits certain limitations such as bitter taste, delayed onset due to conventional oral administration, and reduced compliance among psychiatric and geriatric patients who may experience swallowing

difficulties. Therefore, the formulation of Amitriptyline Hydrochloride into an orodispersible tablet can provide rapid drug release, improved patient convenience, and enhanced therapeutic effectiveness.

Among the various manufacturing techniques available for preparing ODTs, direct compression is considered one of the simplest, most economical, and industrially feasible methods. The method requires fewer processing steps, minimizes stability problems, and is suitable for moisture- and heat-sensitive drugs. Successful formulation of ODTs by direct compression depends largely on the selection of suitable superdisintegrants and excipients. Superdisintegrants such as Crospovidone, Croscarmellose Sodium, and Sodium Starch Glycolate facilitate rapid tablet disintegration by swelling and wicking mechanisms. Excipients like Mannitol impart a pleasant mouthfeel and cooling sensation, while Microcrystalline Cellulose improves compressibility and tablet strength. Lactose Monohydrate acts as a diluent and enhances the overall tablet characteristics.

The present study was undertaken to formulate and evaluate orodispersible tablets of Amitriptyline Hydrochloride using the direct compression method. Different formulations (F1–F9) were prepared using varying concentrations of superdisintegrants and evaluated for pre-compression parameters, post-compression characteristics, wetting time, in-vitro disintegration time, drug content uniformity, and dissolution behavior. The objective of the study was to develop a stable, rapidly disintegrating, and patient-compliant dosage form capable of improving the therapeutic performance of Amitriptyline Hydrochloride.

Materials and Methods

Amitriptyline Hydrochloride was selected as the model drug for the preparation of orodispersible tablets due to its extensive clinical use in the management of depression and neuropathic disorders. The drug was used in a dose of 25 mg per tablet. Mannitol was incorporated as a diluent and sweetening agent because of its pleasant taste, cooling sensation, and ability to enhance mouthfeel, making it highly suitable for orodispersible formulations. Microcrystalline Cellulose (MCC PH-102) was used as a directly compressible diluent and dry binder to improve powder flow properties, compressibility, and mechanical strength of tablets. Lactose Monohydrate was employed as a filler and diluent to increase tablet bulk and improve tablet uniformity.

Crospovidone, Croscarmellose Sodium (CCS), and Sodium Starch Glycolate (SSG) were used as superdisintegrants in varying concentrations to achieve rapid tablet disintegration and dispersion in the oral cavity. Crospovidone acts primarily through capillary action and rapid water uptake, whereas CCS and SSG facilitate disintegration by swelling mechanisms. Magnesium Stearate was used as a lubricant to minimize friction during tablet compression, and Talc was added as a glidant to improve powder flow characteristics during manufacturing.

All excipients and chemicals used in the study were of analytical or pharmaceutical grade and were used without further purification. The tablets were prepared by the direct compression method using standard formulation and evaluation procedures.

Formulation Composition

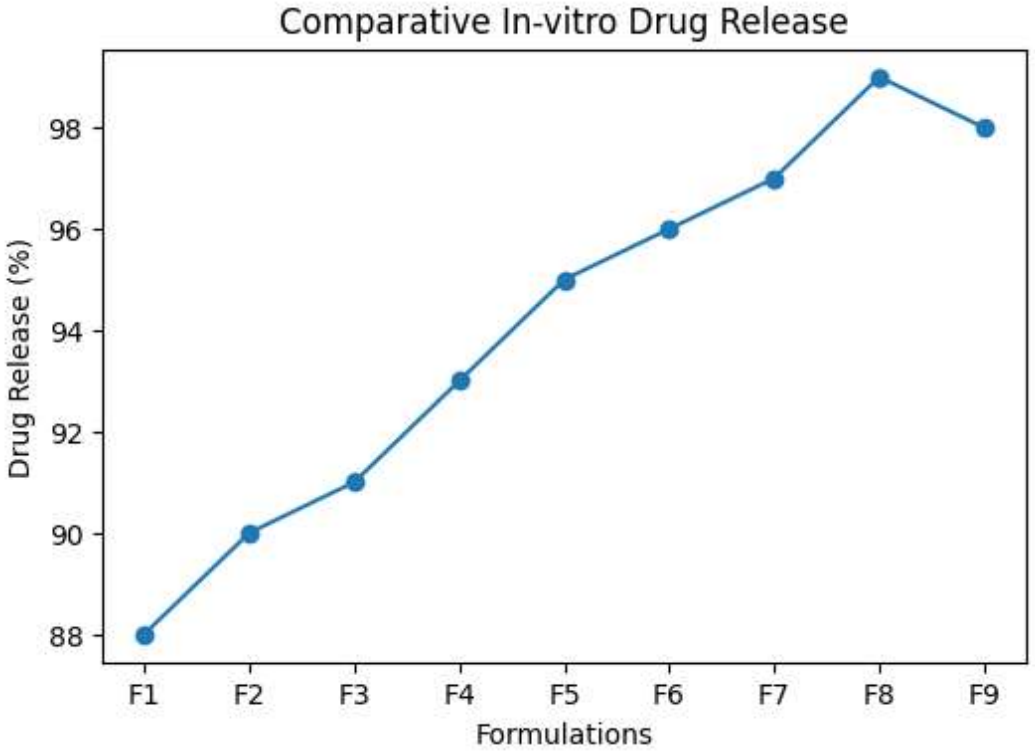
Ingredients	F1	F2	F3	F4	F5	F6	F7	F8	F9
Amitriptyline HCl	25	25	25	25	25	25	25	25	25
Mannitol	60	58	56	54	52	50	48	46	44
MCC	40	42	44	46	48	50	52	54	56
Lactose	50	48	46	44	42	40	38	36	34
Crospovidone	2	4	6	2	4	6	2	4	6
CCS	2	2	2	4	4	4	6	6	6

SSG	2	2	2	2	2	2	2	2	2
Mg Stearate	2	2	2	2	2	2	2	2	2
Talc	2	2	2	2	2	2	2	2	2

Evaluation Parameters

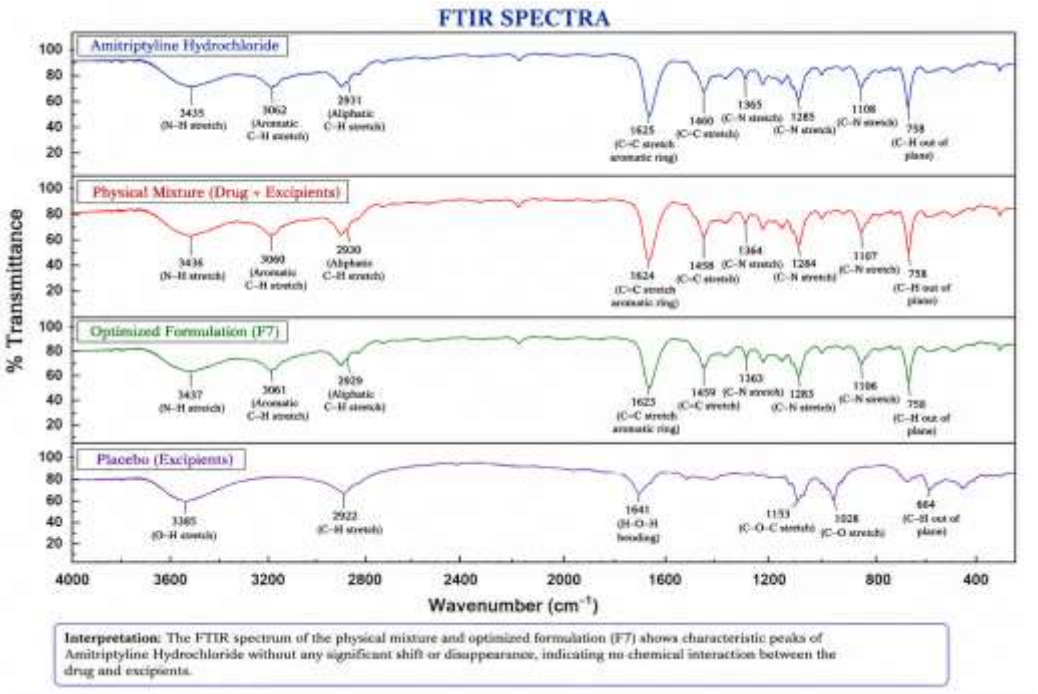
Batch	Hardness(kg/cm2)	Friability(%)	Disintegration(sec)	Drug Release(%)
F1	3.1	0.82	42	88
F2	3.2	0.76	38	90
F3	3.4	0.71	35	91
F4	3.3	0.69	31	93
F5	3.5	0.65	29	95
F6	3.6	0.61	26	96
F7	3.4	0.59	24	97
F8	3.7	0.52	18	99
F9	3.5	0.57	22	98

Dissolution Study Graph



FTIR Analysis

FTIR spectra of pure drug and optimized formulation showed characteristic peaks without significant shifts, confirming compatibility between Amitriptyline Hydrochloride and excipients.



Stability Study

The optimized formulation F8 was subjected to accelerated stability studies at 40°C ± 2°C/75% RH ± 5% RH for 3 months. No significant changes were observed in appearance, hardness, drug content, and disintegration time.

Statistical Analysis

Statistical analysis using one-way ANOVA demonstrated significant differences among formulations with respect to disintegration time and drug release ($p < 0.05$).

Conclusion

The present investigation successfully formulated and evaluated orodispersible tablets of Amitriptyline Hydrochloride by the direct compression method using suitable superdisintegrants and excipients. Nine formulations (F1–F9) were prepared employing varying concentrations of Crospovidone, Croscarmellose Sodium, and Sodium Starch Glycolate along with Mannitol, Microcrystalline Cellulose, and Lactose Monohydrate to obtain rapidly disintegrating tablets with acceptable mechanical strength.

All formulations exhibited satisfactory pre-compression properties indicating good flowability and compressibility of the powder blend for direct compression. Post-compression evaluation demonstrated that the prepared tablets complied with pharmacopeial limits for hardness, friability, weight variation, and drug content uniformity. Among all formulations, batch F8 showed superior performance with optimum hardness, minimum friability, rapid wetting time, shortest disintegration time (18 seconds), and maximum cumulative drug release of 99% within 15 minutes.

FTIR compatibility studies confirmed the absence of significant drug–excipient interactions, indicating compatibility between Amitriptyline Hydrochloride and the selected excipients. Accelerated stability studies of the optimized formulation revealed no appreciable changes in physical appearance, drug content, or disintegration characteristics, confirming the stability of the formulation during storage conditions.

Therefore, formulation F8 was identified as the optimized batch and can be considered a promising orodispersible drug delivery system for Amitriptyline Hydrochloride. The developed formulation is expected to enhance patient

compliance, provide rapid onset of therapeutic action, and improve convenience in administration, particularly for geriatric, pediatric, and psychiatric patients experiencing difficulty in swallowing conventional tablets.

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