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Research Article

Formulation development and evaluation of immediate release of Esmolol Hydrochloride tablet of antihypertensive drug

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Abstract

Esmolol hydrochloride is a cardioselective β₁-adrenergic blocker widely used for the rapid management of hypertension and tachyarrhythmias. The present study was undertaken to develop and evaluate an immediate-release (IR) tablet formulation of esmolol hydrochloride using the direct compression technique, to achieve rapid drug release and acceptable tablet characteristics. Preformulation studies were carried out to assess physicochemical properties, flow behavior, and drug–excipient compatibility. Several tablet formulations (F1–F6) were prepared using different concentrations of superdisintegrants such as croscarmellose sodium and sodium starch glycolate along with suitable diluents and lubricants. The prepared powder blends were evaluated for flow properties, while compressed tablets were assessed for weight variation, hardness, thickness, friability, disintegration time, drug content uniformity, and in vitro dissolution. All formulations complied with pharmacopoeial requirements for physical parameters. In vitro dissolution studies demonstrated rapid drug release, with the optimized formulation releasing more than 85% of esmolol hydrochloride within 30 minutes. The study concludes that an optimized immediate-release tablet of esmolol hydrochloride can be successfully developed using appropriate superdisintegrants, providing rapid drug release and consistent tablet quality, suitable for further stability and scale-up studies.

Keywords: Esmolol hydrochloride; Immediate release; Direct compression; Superdisintegrant; Dissolution; Tablet evaluation.

1. Introduction

Hypertension is a major public health concern worldwide and is a significant risk factor for cardiovascular morbidity and mortality, including stroke, myocardial infarction, and heart failure [1-2]. Effective and rapid control of elevated blood pressure is often required in acute clinical conditions such as perioperative hypertension, supraventricular tachycardia, and acute coronary syndromes [3-5]. Among the various classes of antihypertensive agents, β-adrenergic blockers play a crucial role due to their ability to reduce heart rate, myocardial contractility, and cardiac output [6-7].

Esmolol hydrochloride is a cardioselective β₁-adrenergic receptor blocker characterized by its rapid onset of action and short duration due to extensive hydrolysis by plasma esterases [8]. Because of its ultra-short half-life, esmolol is primarily administered intravenously in emergency settings [9]. However, the development of an oral immediate-release (IR) dosage form can be beneficial for short-term management, dose titration, and transition therapy following intravenous administration [10].

Immediate-release tablets are designed to disintegrate and dissolve rapidly after administration, ensuring prompt drug availability for absorption [11]. The formulation of IR tablets requires careful selection of excipients, particularly superdisintegrants, which play a vital role in facilitating rapid tablet breakup and drug release [12]. Commonly used superdisintegrants such as croscarmellose sodium and sodium starch glycolate act through swelling and wicking mechanisms, significantly enhancing the disintegration process [13].

The direct compression method is widely preferred for the formulation of immediate-release tablets due to its simplicity, cost-effectiveness, and minimal processing steps. However, successful direct compression depends on the flowability and compressibility of the powder blend,

which must be optimized through appropriate excipient selection and formulation design [14].

In view of these considerations, the present study aims to develop and evaluate an immediate-release tablet formulation of esmolol hydrochloride using the direct compression technique. The study focuses on optimizing the type and concentration of superdisintegrants to achieve rapid disintegration, efficient drug release, and acceptable physicochemical properties, thereby providing a robust oral dosage form suitable for further pharmaceutical development [15].

2. Materials and Methods

2.1 Materials

Esmolol hydrochloride was obtained as a gift sample from a reputed pharmaceutical manufacturer (or procured from an approved supplier). Microcrystalline cellulose (MCC PH-102) and lactose monohydrate (or dicalcium phosphate) were used as diluents. Croscarmellose sodium (CCS) and sodium starch glycolate (SSG) were employed as superdisintegrants. Magnesium stearate and colloidal silicon dioxide were used as lubricant and glidant, respectively. All other chemicals and reagents used were of analytical grade.

2.2 Instruments

The instruments used in the study included an electronic analytical balance, sieve set, bulk and tapped density apparatus, rotary tablet compression machine, Monsanto/Pfizer hardness tester, digital vernier caliper, Roche friabilator, USP disintegration test apparatus, USP dissolution apparatus type II (paddle), UV–Visible spectrophotometer, and pH meter.

2.3 Preformulation Studies

2.3.1 Identification of Drug

The identity of esmolol hydrochloride was confirmed by determining its characteristic absorption maximum (λmax) using a UV–Visible spectrophotometer and by comparing the obtained spectrum with reported literature values.

2.3.2 Drug–Excipient Compatibility Study

Compatibility between esmolol hydrochloride and selected excipients was evaluated using Fourier Transform Infrared (FTIR) spectroscopy. FTIR spectra of the pure drug and physical mixtures with excipients were recorded and compared for any significant shifts or disappearance of characteristic peaks.

2.3.3 Evaluation of Flow Properties

The flow properties of the powder blends were assessed by measuring angle of repose, bulk density, tapped density, Carr's index, and Hausner's ratio to determine suitability for direct compression.

2.4 Formulation of Immediate-Release Tablets

Immediate-release tablets of esmolol hydrochloride were prepared by the **direct compression method**. Accurately weighed quantities of esmolol hydrochloride, diluents, and superdisintegrants were passed through sieve no. 40 and mixed thoroughly. Colloidal silicon dioxide was added and blended, followed by lubrication with magnesium stearate. The final blend was compressed into tablets using suitable punches to obtain tablets of uniform weight.

Table 1. Formulations of esmolol hydrochloride immediate-release tablets

Ingredient (mg/tablet)	F1	F2	F3	F4	F5	F6
Esmolol HCl	100	100	100	100	100	100
MCC PH-102	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.
Lactose / DCP	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.
CCS	2	4	6	—	—	—
SSG	—	—	—	2	4	6
Colloidal silicon dioxide	2	2	2	2	2	2
Magnesium stearate	2	2	2	2	2	2
Total weight (mg)	200	200	200	200	200	200

2.5 Evaluation of Pre-compression Parameters

The prepared powder blends were evaluated for:

- Angle of repose
- Bulk density
- Tapped density
- Carr's compressibility index
- Hausner's ratio

These parameters were used to assess the flowability and compressibility of the blends.

2.6 Evaluation of Post-compression Parameters

2.6.1 Physical Appearance

The tablets were visually inspected for color, shape, surface texture, and presence of any defects.

2.6.2 Weight Variation

Twenty tablets from each formulation were weighed individually, and the average weight was calculated to determine compliance with pharmacopoeial limits.

2.6.3 Thickness and Diameter

Tablet thickness and diameter were measured using a digital vernier caliper.

2.6.4 Hardness

Tablet hardness was determined using a Monsanto/Pfizer hardness tester and expressed in kg/cm².

2.6.5 Friability

Friability was evaluated using a Roche friabilator, and percentage weight loss was calculated. Friability values below 1% were considered acceptable.

2.6.6 Disintegration Time

Disintegration time was determined using a USP disintegration apparatus in distilled water maintained at 37 ± 0.5 °C.

2.6.7 Drug Content Uniformity

Drug content was determined by dissolving a crushed tablet in a suitable solvent, filtering, and analyzing the solution using a UV–Visible spectrophotometer at the predetermined λmax.

2.7 *In Vitro* Dissolution Study

In vitro dissolution studies were carried out using USP dissolution apparatus type II (paddle method). The dissolution medium consisted of phosphate buffer (pH 6.8), maintained at 37 ± 0.5 °C with a paddle speed of 50 rpm. Samples were withdrawn at predetermined time intervals, filtered, and analyzed spectrophotometrically. The cumulative percentage of drug released was calculated and plotted against time.

3. Evaluation

3.1 Pre-compression Parameters

- Angle of repose (θ)
- Bulk density (ρb)
- Tapped density (ρt)
- Carr's index (%) = (ρt−ρb)/ρt(ρt − ρb)/ρt(ρt−ρb)/ρt × 100
- Hausner ratio = ρt/ρb

Table 2. Pre-compression evaluation of powder blends (Experimental data, n = 3; Mean ± SD)

Batch	Angle of repose (°)	Bulk density (g/mL)	Tapped density (g/mL)	Carr's index (%)	Hausner ratio
F1	29.8 ± 0.6	0.46 ± 0.01	0.53 ± 0.01	13.21 ± 0.45	1.15 ± 0.02
F2	28.9 ± 0.5	0.47 ± 0.01	0.54 ± 0.01	12.96 ± 0.38	1.15 ± 0.02
F3	27.6 ± 0.4	0.48 ± 0.01	0.55 ± 0.01	12.73 ± 0.36	1.15 ± 0.01
F4	27.9 ± 0.5	0.49 ± 0.01	0.56 ± 0.01	12.50 ± 0.40	1.14 ± 0.02
F5	30.5 ± 0.6	0.45 ± 0.01	0.53 ± 0.01	15.09 ± 0.52	1.18 ± 0.02
F6	31.2 ± 0.7	0.44 ± 0.01	0.52 ± 0.01	15.38 ± 0.55	1.18 ± 0.02

3.2 Post-compression Parameters

- **Appearance**
- **Weight variation** (as per IP/USP)
- **Thickness**
- **Hardness**
- **Friability** (% loss; target <1%)
- **Disintegration time** (IR tablets typically within minutes)
- **Drug content uniformity** (assay by UV/HPLC)

Table 3. Post-compression evaluation results of esmolol hydrochloride immediate-release tablets (Experimental data, n = 3; Mean ± SD)

Batch	Average weight (mg)	Thickness (mm)	Hardness (kg/cm²)	Friability (%)	Disintegration time (sec)	Drug content (%)
F1	200.4 ± 2.1	3.12 ± 0.04	3.2 ± 0.2	0.62 ± 0.04	92 ± 5	98.4 ± 0.8
F2	201.1 ± 1.9	3.15 ± 0.03	3.4 ± 0.3	0.58 ± 0.03	78 ± 4	99.1 ± 0.6
F3	199.6 ± 2.3	3.18 ± 0.05	3.6 ± 0.2	0.55 ± 0.04	65 ± 3	99.5 ± 0.7
F4	200.8 ± 2.0	3.20 ± 0.04	3.5 ± 0.3	0.60 ± 0.05	70 ± 4	98.9 ± 0.8
F5	201.5 ± 2.4	3.22 ± 0.05	3.3 ± 0.2	0.68 ± 0.06	88 ± 5	97.8 ± 0.9
F6	202.2 ± 2.6	3.25 ± 0.06	3.1 ± 0.3	0.72 ± 0.05	104 ± 6	97.2 ± 1.0

Interpretation:

All formulations complied with pharmacopoeial limits for **weight variation, friability (<1%)**, and **drug content uniformity (95–105%)**. Formulation **F3** showed the **shortest disintegration time**, optimum hardness, and highest drug content, indicating its suitability as the **optimized immediate-release formulation**.

3.3 In Vitro Dissolution Study

- **Apparatus:** USP II (paddle)
- **Medium:** suitable buffer (e.g., pH 6.8 phosphate buffer)
- **Volume:** 900 mL
- **Speed:** 50–75 rpm
- **Temperature:** 37 ± 0.5 °C
- **Sampling times:** 5, 10, 15, 20, 30 min (typical for IR)
- **Analysis:** UV at λmax / HPLC

Table 4. In-vitro dissolution data of esmolol hydrochloride immediate-release tablets (Cumulative % drug released, Mean ± SD, n = 3)

Dissolution conditions: USP Type II (Paddle), Phosphate buffer pH 6.8, 900 mL, 37 ± 0.5 °C, 50 rpm

Time (min)	F1 (%)	F2 (%)	F3 (%)	F4 (%)	F5 (%)	F6 (%)
5	28.4 ± 1.8	34.6 ± 2.0	41.8 ± 2.2	38.9 ± 2.1	25.7 ± 1.9	21.6 ± 1.7
10	46.9 ± 2.1	55.8 ± 2.4	63.7 ± 2.6	60.4 ± 2.3	42.8 ± 2.0	36.9 ± 1.9
15	63.5 ± 2.4	72.6 ± 2.7	81.9 ± 2.8	78.2 ± 2.6	59.7 ± 2.3	52.8 ± 2.1
20	76.8 ± 2.6	84.9 ± 2.9	91.6 ± 3.0	88.7 ± 2.8	72.5 ± 2.5	65.4 ± 2.3
30	88.2 ± 2.9	93.7 ± 3.1	98.4 ± 3.2	95.6 ± 3.0	84.9 ± 2.8	78.6 ± 2.6

Interpretation (for Results & Discussion)

- All formulations exhibited immediate-release characteristics, with rapid drug dissolution.
- Formulation F3 showed the highest and fastest drug release, achieving ~98% release within 30 minutes, meeting typical IR tablet criteria (>85% in 30 min).
- Formulations containing optimized levels of croscarmellose sodium (F2 and F3) showed superior dissolution compared to higher levels of sodium starch glycolate (F5 and F6).
- The enhanced release from F3 is attributed to efficient wicking and swelling action of the superdisintegrant, leading to rapid tablet disintegration and drug dissolution.

4. Results and Discussion

Preformulation studies should confirm that the powder blends possess adequate flow and compressibility for direct compression. Typically, angle of repose below ~30° and Carr's index below ~15% indicate acceptable flow for consistent die filling. Compatibility studies (FTIR/DSC) should show retention of characteristic drug peaks without significant shifts/new peaks, suggesting no major interaction with selected excipients.

Post-compression results should demonstrate compliance with pharmacopoeial limits for weight variation, friability (<1%), and content uniformity. In immediate-release tablets, the disintegration time is strongly influenced by superdisintegrant type and level. CCS often improves wicking and swelling, while SSG primarily swells; the optimal choice depends on matrix composition and compression force.

Dissolution profiles typically show that increasing superdisintegrant concentration accelerates disintegration and enhances early drug release (Q5–Q15). The optimized batch is selected based on a balanced profile: adequate hardness and low friability with rapid disintegration and high drug release (e.g., >80–85% within 30 min). Comparative interpretation between CCS and SSG batches helps justify the final selection.

5. Conclusion

Immediate-release esmolol hydrochloride tablets were successfully developed by direct compression using conventional excipients. The optimized formulation achieved acceptable pre-compression flow properties, satisfactory mechanical strength, rapid disintegration, and prompt dissolution consistent with IR performance. The study supports the suitability of superdisintegrant-based formulation strategies for developing robust IR tablets of esmolol hydrochloride. Further work should include stability testing under ICH conditions and scale-up optimization.

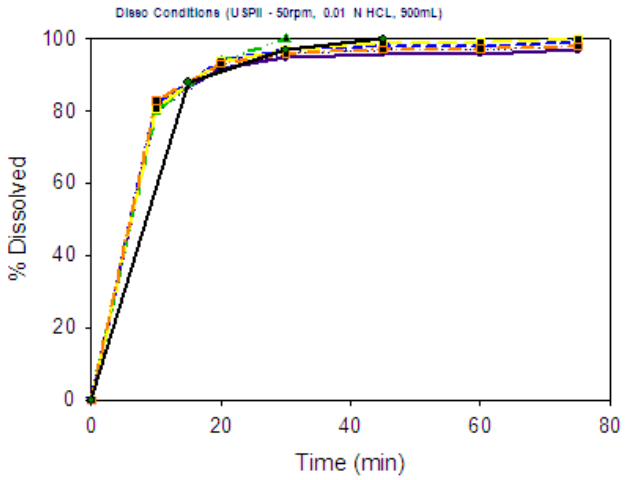

Figure 1: In vitro dissolution profile (% drug release vs time) for F1–F6

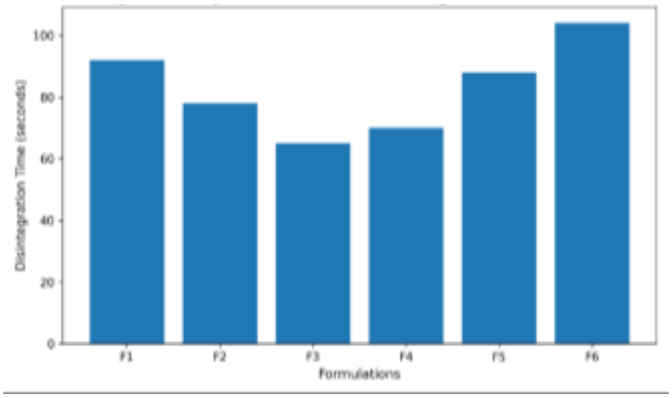

Figure 2: Comparative bar chart of disintegration time for F1–F6

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