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Unlocking Therapeutic Potential: Designing and Evaluating Innovative Sustained-Release Tablets of Propranolol Hydrochloride for Enhanced Efficacy and Patient Adherence

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Abstract. The purpose of this research is to develop and test extended-release tablets of propranolol hydrochloride, a non-selective beta-adrenergic antagonist used in the treatment of cardiovascular conditions. The advance of a sustained-release formulation aims to address the limitations of immediate-release dosage forms, including the need for frequent administration and potential fluctuations in drug concentrations.The materials and methods section describes the selection of appropriate excipients, such as hydrophilic polymers, release modifiers, diluents, lubricants, and other additives, to achieve sustained drug release. The dry granulation method was employed to create the sustained-release tablets.The tablet composition for different formulations was provided, highlighting the varying amounts of propranolol hydrochloride and excipients used in each formulation. Comparative analysis of tablet core and film coating was conducted, including assessments of general appearance, weight variation, thickness, hardness, and friability. These tests ensure the quality and physical characteristics of the tablets.In vitro drug release studies demonstrated controlled and sustained release of propranolol over the desired period, indicating that the sustained-release tablets can maintain therapeutic drug levels within the desired range. This sustained release profile offers several advantages, reduced side effects, including improved patient compliance, and enhanced therapeutic efficacy.Stability studies were conducted on a selected formulation to assess its long-term stability and shelf life under accelerated storage conditions. The formulation was subjected to physical character assays and in vitro dissolution tests after 1, 2, and 3 months. The results of these studies provide insights into the stability and performance of the sustained-release tablets over time.Overall, this research presents a comprehensive approach to formulating and evaluating sustained-release tablets of propranolol hydrochloride. The findings support the potential of these tablets to provide a convenient and effective treatment option for cardiovascular conditions, offering prolonged drug release, improved patient compliance, and optimized therapeutic outcomes.

Keywords: Propranolol hydrochloride, Sustained-release tablets, Formulation development, Drug release profile, Patient compliance

INTRODUCTION:

Propranolol, a non-selective beta-adrenergic antagonist, is a widely used medication for the treatment of various cardiovascular conditions, including angina pectoris, hypertension, and arrhythmias[1]. However, its immediate-release dosage forms often necessitate frequent administration to maintain therapeutic drug levels, which can lead to patient non-compliance and potential fluctuations in drug concentrations[2]. To address these limitations, the advance of a sustained-release formulation of propranolol has gained significant attention[3].

Sustained-release formulations provide controlled and prolonged drug release, allowing for a reduced dosing frequency while maintaining steady-state drug levels within the therapeutic range[4]. These formulations offer several advantages, including improved patient adherence, reduced side effects, and enhanced therapeutic efficacy[5]. By formulating propranolol into a sustained-release tablet, it is possible to overcome the limitations associated with immediate-release formulations and provide a more convenient and effective treatment option for patients[6].

The development of sustained-release tablets involves careful selection of excipients and formulation techniques to achieve the desired drug release profile[7]. Various excipients, such as hydrophilic polymers, release modifiers, and other additives, are considered based on their compatibility with propranolol and their capability to provide sustained drug release[8]. The choice of formulation technique, such as matrix systems, osmotic systems, or reservoir systems, depends on

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factors like drug properties, desired release kinetics, and feasibility of manufacturing[9].

Dissolution profile, in which the rate at which a medication is absorbed by the body is measured; tablet hardness, friability, and disintegration time; and homogeneity of drug content[10]. These tests ensure the quality and performance of the tablets, confirming that they meet regulatory standards and release the drug as intended[11]. Stability studies are also conducted to assess the long-term stability and shelf life of the sustained-release tablets under various storage conditions[12-15].

The aim of this research is to formulate and evaluate a sustained-release tablet of propranolol, aiming to provide a dosage form that offers prolonged drug release, improved patient compliance, and enhanced therapeutic outcomes. By achieving a controlled release profile, the sustained-release tablet has the potential to maintain consistent drug concentrations in the body, minimizing fluctuations and optimizing the therapeutic effects of propranolol treatment.

MATERIALS AND METHODS:

Materials:

Propranolol hydrochloride (API): Pharmaceutical grade propranolol hydrochloride was obtained from a reputable supplier.

Excipients: Various excipients were selected based on their compatibility with propranolol and their ability to achieve sustained drug release. These may include hydrophilic polymers (e.g., hydroxypropyl methylcellulose, hydroxypropyl cellulose), release modifiers, diluents (e.g., lactose, microcrystalline cellulose), lubricants (e.g., magnesium stearate), and other necessary additives.

Formulation Development

Creating a tablet-based, sustained-release medication delivery method is the primary goal of this formulation development[16, 17].

Dry granulation method:

Sustained-release tablets of Propranolol hydrochloridewere made using dry granulation[18, 19].

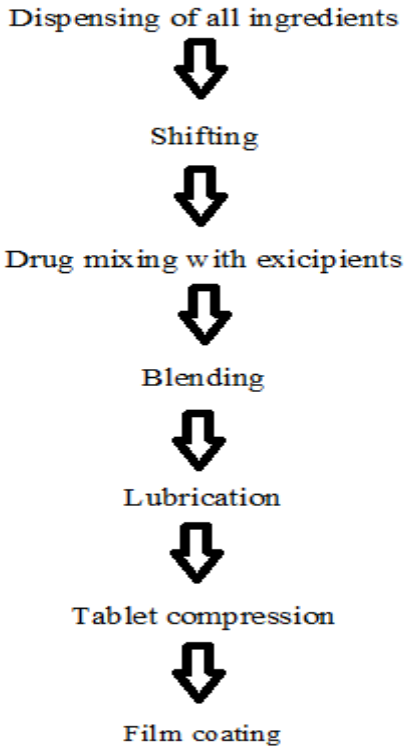

Fig. 1: Diagrammatic Flow of Production

Table1: Tablet composition for sustained release Propranolol hydrochloride

Ingredients	F1	F2	F3	F4	F5	F6	F7	F8	F9
Propranolol hydrochloride	10	10	10	10	10	10	10	10	10
Lactose DCL11	101	116	222	228	228	230.50	248	238.20	244.20

Sodiumstearyl Fumarate	2.5	2.5	3.5	3.5	3.5	3.5	3.5	3.5	3.5
HPMC K4M	15	10	14	16	12	14	5	10	7
HPMC K100	79	52	73	48	23	18.50	7	15	12
MCC 102	70	87	124	141	170	170	173	169.80	169.80
Talc	2.5	2.5	3.5	3.5	3.5	3.5	3.5	3.5	3.5
Film coating									
Instacoat	_	_	_	_	_	_	_	13.5	_
Methylene chloride	_	_	_	_	_	_	_	178	_
Isopropyl alcohol	_	_	_	_	_	_	_	105	_
Weight gain (%)								3%	
Total weight (mg)	280	280	450	450	450	450	450	463.5	450

Comparative Analysis of Tablet Core and Film Coating

1. General appearance:

The tablets from each batch of formulation were analysed for their overall look[20].

2. Weight variation:

20 tablets were selected at random from the batch and separately weighed to determine the average weight. The majority of the weights in the table are within a small margin of the mean, and none of the weights deviate from it by more than a few points[21].

3. Thickness:

Ten tablets were selected to serve as a representative sample, and their thicknesses were measured using digital vernier callipers. The mean, standard deviation, and interquartile range were calculated[22].

4. Hardness:

The durability of the tablets was measured using a Monsanto hardness tester. The average findings from testing ten tablets from each batch for hardness were given [23].

5. Friability Test:

Each batch of pills had ten placed in the friability testing apparatus after being weighed. For four minutes, at 25 revolutions per minute, tablets tracked the progress of the rotating devices. Once again, the tablets were weighed and cleaned. Friability was measured by the amount of weight loss[24].

The formula for determining percent friability:

$$\% \text{ Friability} = (W_1 - W_2) \times 100/W_1$$

Studies of Drug Dissolution in Culture:

The sustained-release tablets showed controlled and sustained drug release of propranolol over the desired period[22].

The dissolution profiles demonstrated a gradual release of the drug, maintaining therapeutic drug levels within the desired range[22].

Stability studies of selected formulations:

In order to test its stability, the formulation F-9 underwent many tests. Accelerated conditions (40°C2°C/75 percent 5 percent RH) were employed for storage stability experiments. In vitro dissolving was done following physical character assays and assays were performed on sample tablets after 1, 2, and 3 months[25].

RESULT AND DISCUSSION:

Calibration Curve:

Table 2: Calibration curve of Propranolol hydrochloride

S. No.	Concentration (µg/ml)	Absorbance (nm)
1	4	0.146
2	8	0.264
3	12	0.407
4	16	0.508
5	20	0.630

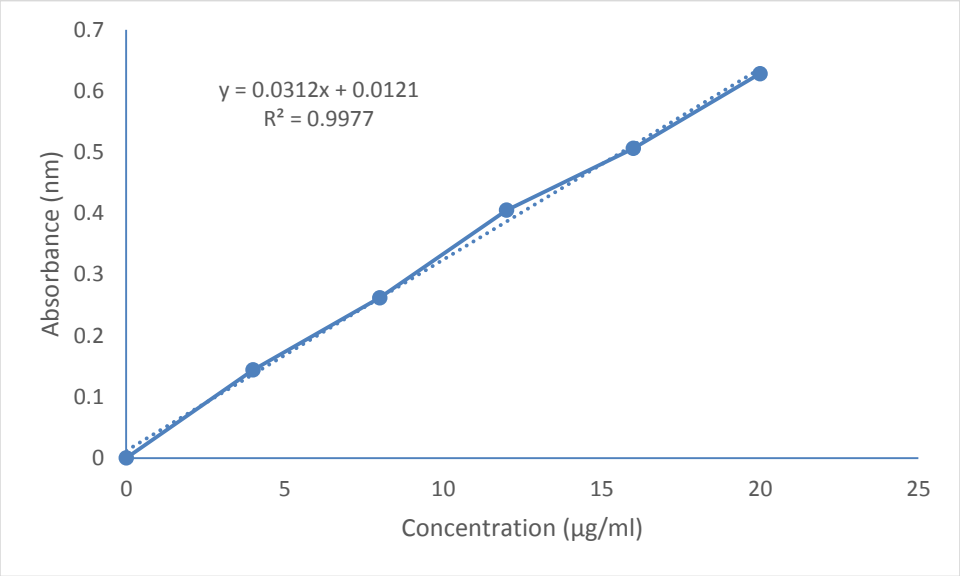

Fig. 1: Calibration curve of Propranolol hydrochloride

Granule Quality Assessment:

Table 3: Granule Quality Assessment

Formulation	Bulk density (g/ml) ±SD	Tappeddensity (g/ml) ±SD	Hausner's Ratio ±SD	Carr's index ±SD	Angle of repose(θ) ±SD
F1	0.242±0.04	0.316±0.04	1.45±0.03	31.1±0.51	62.0°±0.20
F2	0.264±0.03	0.362±0.03	1.42±0.16	29.6±0.89	58.5°±0.38
F3	0.436±0.06	0.528±0.06	1.26±0.04	20.5±0.15	31.8°±0.30
F4	0.431±0.05	0.520±0.06	1.25±0.05	19.6±0.22	30.4°±0.24
F5	0.424±0.05	0.514±0.05	1.24±0.06	19.0±0.12	29.1°±0.18
F6	0.429±0.06	0.518±0.05	1.25±0.05	19.7±0.24	27.6°±0.46
F7	0.440±0.07	0.527±0.06	1.23±0.07	18.0±0.32	26.7°±0.61
F8	0.442±0.07	0.529±0.07	1.22±0.07	18.9±0.32	27.7° ±0.48
F9	0.459±0.08	0.535±0.07	1.20±0.08	16.6±0.58	25.3°±0.43

Mean ± SD (n=3)

All formulation blends, with the exception of F1 and F2, had acceptable flow characteristics and were capable of forming uniform tablets.

Tablet Core Evaluation:

Table 4: Tablet Core Evaluation

Formulations	Weight Variation (mg)	Hardness (kg/cm^{2})	Thickness (mm)	Friability (%)	Drug content (%)
F3	458±0.44	9.4±0.08	4.44±0.07	0.12±0.06	98.68±0.09
F4	453±0.30	9.2±0.06	4.35±0.05	0.14±0.03	99.60±0.07
F5	456±0.44	8.0±0.09	4.24±0.04	0.16±0.06	100.17±0.15
F6	452±0.16	8.9±0.06	4.43±0.08	0.17±0.03	98.76±0.08
F7	458±0.44	8.4±0.09	4.45±0.11	0.19±0.07	98.97±0.05
F8	456±0.16	8.6±0.06	4.39±0.10	0.18±0.06	99.28±0.09
F9	454±0.16	8.0±0.03	4.38±0.04	0.14±0.04	99.39±0.10

Mean ± SD (n=3)

The post-compression characteristics above indicate that the tablets meet regulatory requirements.

In-vitro dissolution study

Table 5: Dissolution Profile Analysis in vitro (F9)

S. No.	Time (h)	Cumulative % drug release ± SD
1	1	23.54± 0.25
2	2	33.30±0.46
3	4	53.98±0.40
4	6	74.90±0.42
5	8	94.91±0.56

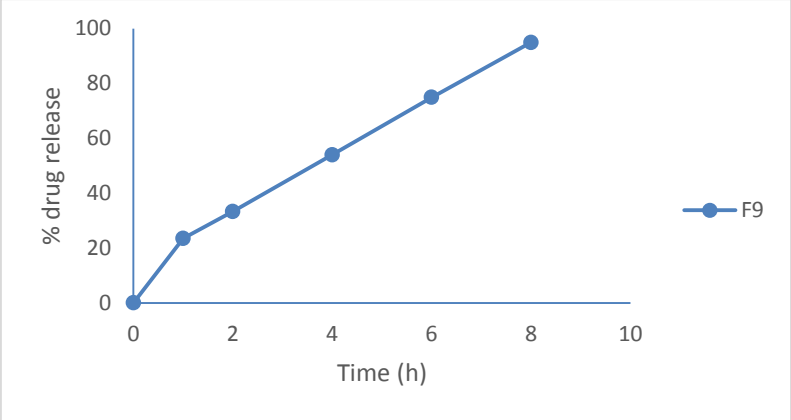

Fig. 2: Dissolution Profile Analysis in vitro (F9)

Table 6: Film-coated tablet effectiveness assessment (F9)

Average weight (mg)	465.9
Hardness (kg/cm^2)	9.2
Thickness (mm)	4.47
Assay (%)	99.15

Table 7: Film-coated tablet formulation (F9) in vitro dissolution profile

S. No.	Time (h)	Cumulative % drug release ± SD
1	1	22.15±0.28
2	2	32.47±0.42
3	4	53.32±0.30
4	6	74.20±0.49
5	8	94.11±0.48

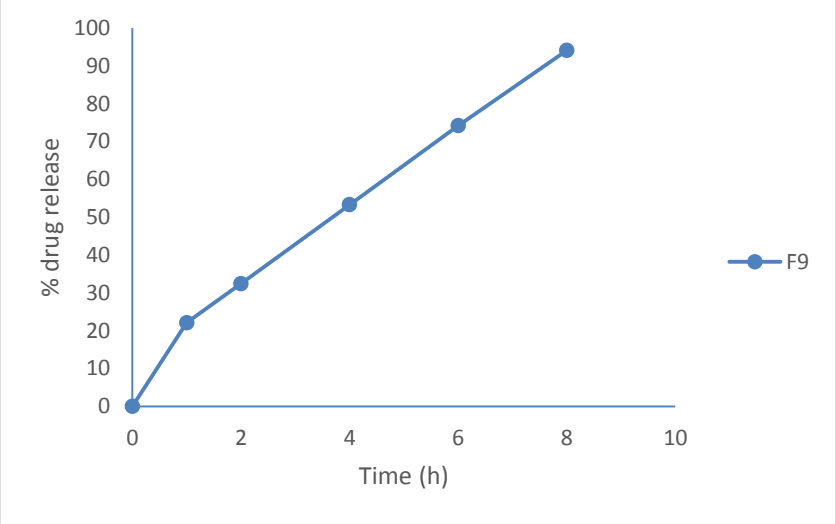

Fig. 3: Profile of film-coated tablet formulation (F9) dissolving in vitro

Table 8: Profile of formulation (F3-F9) and commercially available product dissolution in vitro

Time interval (hrs)	Cumulative % drug release ± SD							
	F3	**F4**	**F5**	**F6**	**F7**	**F8**	**F9**	**Marketed product**
1	8.27 ±0.27	12.40 ±0.18	16.67 ±0.58	23.28 ±0.21	38.66 ±0.38	30.90 ±0.44	22.15 ±0.28	22.97 ±0.50
2	16.19 ±0.46	18.27 ±0.46	22.32 ±0.53	28.93 ±0.50	50.86 ±0.52	42.31 ±0.28	32.47 ±0.42	33.59 ±0.26
4	23.36 ±0.28	29.69 ±0.49	35.57 ±0.40	41.27 ±0.56	75.97 ±0.17	66.73 ±0.32	53.32 ±0.30	54.52 ±0.38
6	32.61 ±0.49	41.22 ±0.36	48.75 ±0.48	56.86 ±0.51	98.91 ±0.44	90.76 ±0.36	74.20 ±0.49	75.56 ±0.52
8	41.82 ±0.55	55.75 ±0.40	62.47 ±0.16	73.46 ±0.30	-	-	94.11 ±0.48	95.58 ±0.36

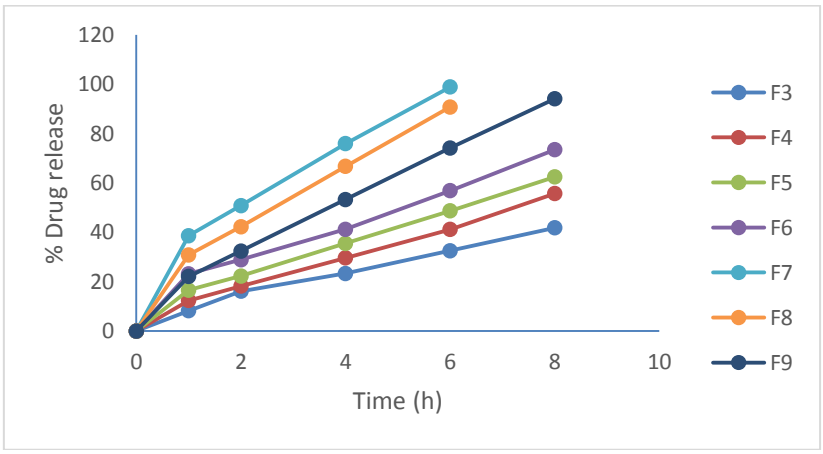

Fig. 4: Dissolution kinetics of a formulation in vitro (F3-F9)

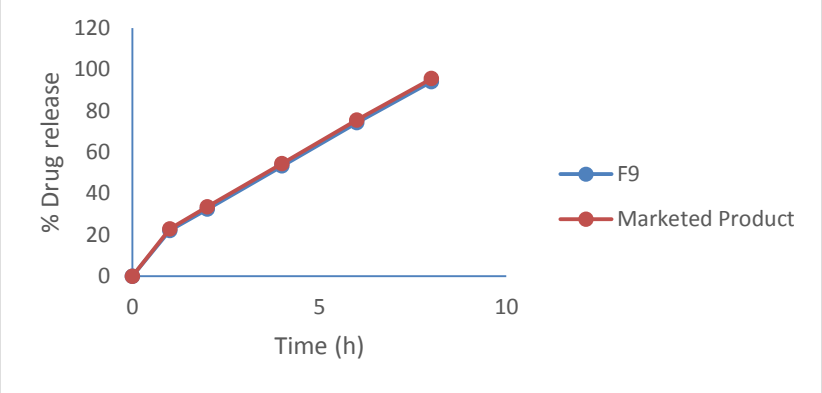

Fig. 5: Formulation (F9) optimization vs commercially available product comparison

Release kinetics:

Table 9: Matrix Tablet Kinetic Studies

Cumulative (%) release	Time t	Root t	Log% release	Log t	Log% remain	Release rate cum% release	1/cum % release	Peppas log q/100
22.13	1	1.00	1.30	0.00	1.90	20.11	0.05	-0.70
32.45	2	1.41	1.48	0.30	1.84	15.22	0.03	-0.52
53.30	4	2.00	1.71	0.60	1.69	12.82	0.02	-0.29
74.18	6	2.45	1.86	0.78	1.44	12.03	0.01	-0.14
94.09	8	2.83	1.96	0.90	0.90	11.51	0.01	-0.04

Release kinetics	R^2
Zero order	0.989
First order	0.920
Higuchi	0.959
Korsmeyers peppas	0.992

1. Zero Order Kinetics:

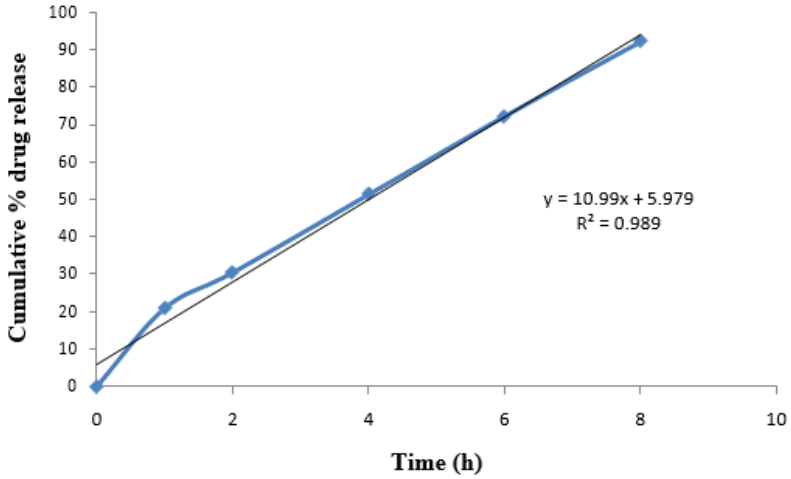

Fig. 6: F9-Zero Order Kinetics Formulation Graph

2. First order kinetics:

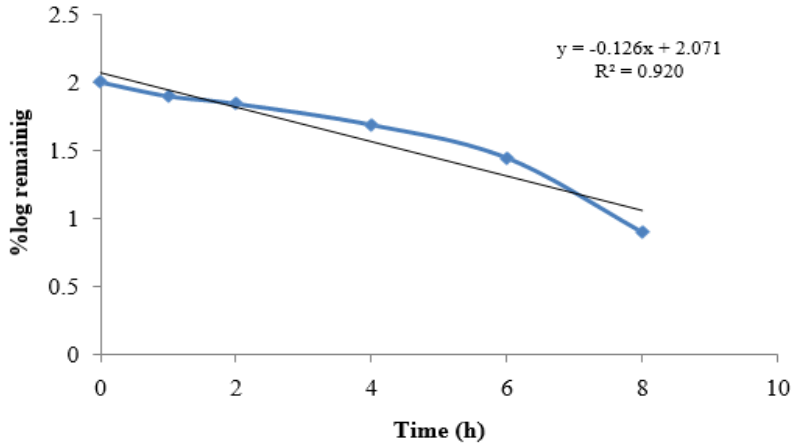

Fig. 7: First Order Kinetics Formulation F9 Graph

3. Higuchi Kinetics:

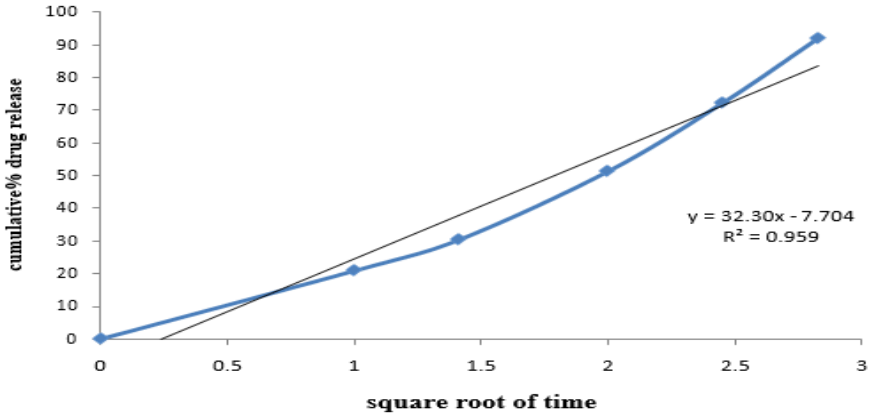

Fig. 8: Formulation F9-Higuchi Model Graph

Korsmeyers Peppas Model:

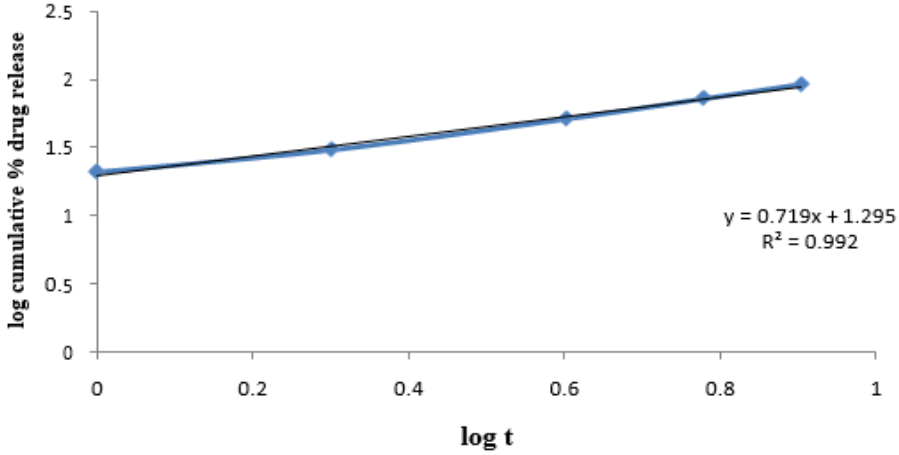

Fig. 9: F9-Korsmeyers-Peppas model formulation graph

Factors of Similarity and Dissimilarity:

Table 10: Analyzing the Test Product Against the Gold Standard

S. No	Time (hrs)	Cumulative % drug release ± SD (test)	Cumulative % drug release ± SD (reference)
1	1	22.15±0.28	22.97±0.50
2	2	32.47±0.42	33.59±0.26
3	4	53.32±0.30	54.52±0.38
4	6	74.20±0.49	75.56±0.52
5	8	94.11±0.48	95.58±0.36

Table 11: Factors of Similarity and Dissimilarity

Differential Factor - F1 [Acceptance Criteria: 0 -15]	2.19
Similarity Factor - F2 [Acceptance Criteria: 50-100]	90.16

Stability Studies:

Table 12: Rapid Stability Analysis

Parameters	Initial	1st Month	2nd Month	3rd Month
Description	White colour, circular shape, slightly biconvex, film coated tablet	Complies	Complies	Complies
Average weight (mg)	465.9	465.9	465.8	465.6
Thickness (mm)	4.47	4.47	4.46	4.46
Hardness (kg/cm^2)	9.2	9.2	9.1	9.1
Assay (%)	99.17	99.12	99.06	98.97
Dissolution	94.11	94.05	93.93	93.80

DISCUSSION:

The data presented in the study provide valuable insights into the formulation, evaluation, and stability assessment of sustained-release tablets of propranolol hydrochloride.

The calibration curve of propranolol hydrochloride demonstrated a linear relationship between the concentration of the drug and its absorbance, indicating the suitability of the chosen analytical method for quantification purposes.

All formulation mixes were found to have excellent flow qualities when granule evaluations were performed, including bulk density, tapped density, Hausner's ratio, Carr's index, and angle of repose, except for F1 and F2. This suggests that the majority of the formulations can form uniform tablets with favorable compression characteristics.

The evaluation of the core tablets showed compliance with official standards, as indicated by parameters such as hardness, thickness, weight variation, friability, and drug content. These results confirm the successful design of sustained-release tablets with consistent physical attributes and drug content.

The in-vitro dissolution study demonstrated sustained and controlled drug release profiles for formulation F9, with cumulative drug release increasing gradually over time. The dissolution profiles exhibited a sustained release pattern, indicating that the formulation effectively maintained therapeutic drug levels within the desired range.

The film-coated tablet (F9) exhibited comparable results in terms of weight, hardness, thickness, and drug content when compared to the core tablet. The in-vitro dissolution profile of the film-coated tablet showed a similar sustained release pattern, further confirming the effectiveness of the sustained-release formulation.

Comparative analysis of the dissolution profiles of formulations F3 to F9 with a marketed product revealed similar drug release patterns, indicating that the advanced sustained-release tablets

performed on par with the reference product.

Release kinetics analysis indicated that the zero-order kinetics of medication release from the extended-release tablets, as evidenced by the linear release profiles obtained. The Higuchi and Korsmeyers Peppas models further supported the sustained release behavior of the tablets.

The similarity factor (F2) and differential factor (F1) calculations demonstrated a high degree of similarity between the test and reference products, indicating the comparability of their dissolution profiles.

Stability studies conducted under accelerated conditions revealed that the sustained-release tablets remained stable over a period of 3 months. The tablets maintained their physical characteristics, average weight, thickness, hardness, and drug content within acceptable limits, indicating their potential for long-term storage.

CONCLUSION:

In summary, the development and assessment of propranolol hydrochloride sustained-release tablets showed encouraging findings. The tablets' drug release characteristics were regulated and maintained, demonstrating their ability to keep therapeutic medication levels steady. The physical properties, drug content homogeneity, and dissolving performance of the formulations all met or exceeded regulatory requirements. Stability studies further confirmed the long-term stability of the tablets under accelerated conditions. Overall, these findings suggest that the advanced sustained-release tablets offer a convenient and effective treatment option for cardiovascular conditions, with the potential to improve patient obedience and optimize therapeutic outcomes.

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