RESEARCH ARTICLE

Formulation and Evaluation of Mouth Dissolving Tablet of Biperiden HCL for Treatments of Parkinson's Disease

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ABSTRACT

Seven formulations were developed using superdisintegrating substances like sodium starch glycolate, crospovidone, and cross-carmellose sodium at different concentrations. Three batches were created by employing varying concentrations of the super disintegration approach, utilizing sodium starch glycolate as the superdisintegrating agent. The batches underwent evaluation regarding sensory characteristics, firmness, breakability, weight consistency, disintegration time in a simulated environment, time is taken for wetting, laboratory tests on drug release within a controlled environment, and assessments of product stability. Fourier transform infrared spectroscopy (FTIR) studies confirmed the absence of drug-excipient interactions. In this examination, mouth-dissolve tablets of biperiden HCL were successfully ready with favorable parameters, including organoleptic properties, hardness (3.2 kg/cm^3), friability (0.23%), weight variation (100 mg), disintegration time within a controlled laboratory environment (17 seconds), wetting time (11 seconds), and *in-vitro* drug release studies (99.80%). The study concluded that the biperiden hydrochloride mouth-dissolving tablet was effectively formulated using the direct compression method, demonstrating improved patient compliance.

Keywords: Biperiden HCL, Super disintegrant crosscarmellose sodium, Crosspovidone, Direct compression method.

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INTRODUCTION

Parkinson's disease, commonly recognized as idiopathic or primary Parkinsonism, hypokinetic rigid syndrome (HRS), or paralysis agitans, is a persistent and progressive movement disorder marked by the deterioration of the nervous system. The disorder, affecting nearly one million individuals in the US, leads to the malfunction and death of essential brain nerve cells known as neurons, primarily in the substantia nigra region. These neurons, responsible for producing dopamine-a chemical crucial for transmitting messages correlated to movement and coordination-gradually diminish as the disease advances. While the underlying factor for Parkinson's remains nameless and there is currently no cure. Several therapeutic choices, encompassing medications and surgical interventions, exist to assist in the management of its symptoms. As the condition progresses, the decreased production of dopamine results in the individual's inability to control movement in a normal manner. [1-2]

MATERIALS AND METHODS

Drug Profile

Biperiden HCL is chemically described as 1-(Bicyclo[2.2.1] hept-5-en-2-yl)-1-phenyl-3-(piperidin-1-yl)propan-1-ol. Functionally, it acts as an antiparkinson agent, belonging to the class of muscarinic antagonists and parasympatholytics. It exhibits practical water solubility and is sparingly soluble in ethanol while being freely dissolved in chloroform. Biperiden HCL melting point of 114°C.A pH is 4.25, and the molecular weight is 347.9 g/mol. [3-5]

Biperiden operates as an inhibitor of muscarinic receptors, demonstrating a relative preference for the M1 receptor subtype. Additionally, it possesses Inhibition of N-methyl-D-aspartate (NMDA) receptor activity.[6-10]

Manufacture of Biperiden Hydrochloride Tablets

Biperiden hydrochloride tablets will be produced in seven batches, labeled A-1 to A-7. Various ratios of a super

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disintegrate, as specified in the Table 1; will be employed while maintaining a consistent total tablet weight of 100 mg across all formulations. [11-17]

Table 1: Bill of material

Components	*A1*	*A2*	*A3*	*A4*	*A5*	*A6*	*A7*
Biperiden	2	2	2	2	2	2	2
Starlac	68	66.5	66.5	66.5	65.5	64	62.5
MCCPH101	20	20	20	20	20	20	20
SSG	-	1.5	-	-	2.5	4	5.5
Crospovidone	-	-	1.5	-	-	-	-
CCS	-	-	-	1.5	-	-	-
Mg stearate (%)	5	5	5	5	5	5	5
Aerosil (%)	3	3	3	3	3	3	3
Orange flavor (%)	2	2	2	2	2	2	2

Table 2: Linearity data of biperiden HCL

S. No	*Beperiden HCL(mcg/ml)*	*Absorbance at 259nm*
1	100	0.167
2	150	0.269
3	200	0.371
4	250	0.473
5	300	0.582
6	350	0.693
7	400	0.790

RESULT AND DISCUSSION

Determination of λ_{max} and Calibration Curve

The standard stock solution was created following the procedure outlined in the methodology section and subjected to UV-visible spectrophotometry. The UV absorption spectrum of biperiden HCL of pH 6.8 solution revealed a peak at 259.0 nm is shown in Figure 1, when compared to the reagent blank, and this finding was utilized for subsequent analysis.

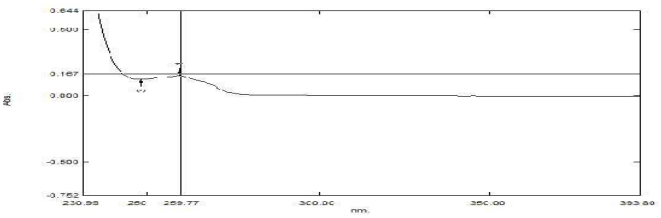

Figure 1: UV spectroscopy of Biperiden HCL of pH 6.8 solution at λ_{max} 259 nm

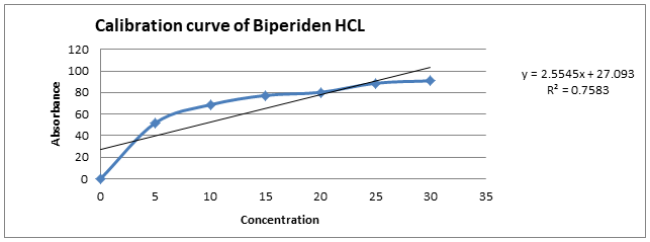

Figure 2: Graphical representation of biperiden HCL in phosphate buffer at pH 6.8

Table 3: Outcome of the assessment of powder blends in formulation batches A1 to A7.

Formulation Batches	*Bulk density (g/mL)*	*Tapped density (g/mL)*	*Carr's index (%)*	*Hausner's ratio*	*Angle of repose (°)*
A1	0.553 ± 0.009	0.617 ± 0.004	10.37 ± 0.77	1.115 ± 0.32	32.61 ± 0.920
A2	0.550 ± 0.0067	0.630 ± 0.004	12.61 ± 0.17	1.145 ± 0.21	31.28 ± 0.395
A3	0.563 ± 0.004	0.644 ± 0.004	12.57 ± 0.25	1.143 ± 0.13	32.54 ± 0.694
A4	0.570 ± 0.003	0.649 ± 0.004	12.17 ± 0.23	1.138 ± 0.15	32.20 ± 0.620
A5	0.572 ± 0.004	0.658 ± 0.004	13.06 ± 0.25	1.150 ± 0.16	32.42 ± 0.412
A6	0.570 ± 0.005	0.660 ± 0.005	13.76 ± 0.75	1.159 ± 0.16	33.08 ± 0.760
A7	0.560 ± 0.067	0.623 ± 0.004	10.11 ± 0.61	1.112 ± 0.31	30.48 ± 0370

Table 4: Outcome of the assessment of formulation batches A1 to A7.

Formulation batches	*Thickness*	*Disintegration time (sec)*	*Wet time (sec)*	*Solidity (kg/cm^3)*	*Mass variation (mg)*	*Friability (%)*
A1	2.51 ± 0.056	42 ± 0.94	36 ± 1.12	3.24 ± 0.057	99.55 ± 2.50	0.495 ± 0.099
A2	2.50 ± 0.055	25 ± 0.622	22 ± 0.34	3.14 ± 0.056	98.55 ± 1.77	0.231 ± 0.057
A3	2.51 ± 0.056	30 ± 0.522	26 ± 0.67	3.18 ± 0.573	100.5 ± 1.84	0.262 ± 0.057
A4	2.51 ± 0.052	31 ± 0.842	27 ± 0.12	3.3 ± 0.057	99.8 ± 1.719	0.297 ± 0.055
A5	2.51 ± 0.054	21 ± 0.452	19 ± 0.42	3.20 ± 0.551	101.15 ± 1.7	0.22 ± 0.151
A6	2.51 ± 0.055	9 ± 0.625	15 ± 0.52	3.22 ± 0.115	102.5 ± 1.79	0.294 ± 0.254
A7	2.50 ± 0.055	17 ± 0.524	11 ± 0.21	3.26 ± 0.057	100 ± 1.77	0.231 ± 0.057

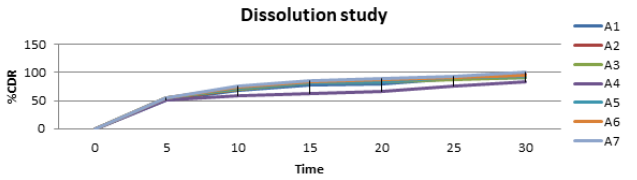

Figure 3: Dissolution study of biperiden HCL from the batches A1 to A7

Table 5: Data for dissolution study of biperiden HCL tablets of batches A1 - A7

Time (min)	*A1*	*A2*	*A3*	*A4*
0	0.00	0.00	0.00	0.00
5	51.97	53.36	54.33	50.73
10	68.72	70.80	70.41	59.03
15	77.36	84.09	82.05	62.01
20	80.24	86.41	84.09	66.31
25	88.69	91.40	86.82	75.66
30	90.89	96.48	91.29	83.96
	A5	A6	A7	
0	0.00	0.00	0.00	
5	54.38	54.40	55.47	
10	72.82	74.80	75.80	
15	82.46	84.39	86.30	
20	84.60	86.40	88.95	
25	90.81	91.89	92.85	
30	92.08	94.15	99.80	

Calibration Curve for Biperiden HCL

The calibration plot and the dataset generated through the method outlined in the method part are presented in Table 2. The statistical analysis demonstrated a statistical measure of the degree of association or relationship between two variables is 0.9979, and the regressed line equation is depicted Figure 2.

The data points of absorbance underwent linear regression analysis. The outcomes for the standard curve in pH 6.8 phosphate buffer include the generation of a linear equation (Y = mx + c) was employed to facilitate the computation of the drug quantity. The assessment is outlined as follows.

Preformulation Studies

Pre-formulation studies were conducted on both biperiden HCL and the excipients.

Melting point

The Biperiden HCL melting point was determined using the capillary pipe method, and the observed melting point for the drug sample was 114ºC. This value is consistent with the documented range of 110 to 115°C, affirming the conformity of the drug sample to established standards and indicating its purity.

Table 7: Characterization of the marketed table.

Development	*Observation*
Physical characteristics	snowy, odorless
width	2.50 ± 0.055mm
Hardness	3.2 ± 0.051(kg/cm^3)
Friability	0.22 ± 0.15%
DT	17 ± 0.50(sec)
Weight variation	100.4 ± 1.74mg
In Vitro Drug Release Studies	98.99%

Table 8: Dissolution for the MDT batch A7 and market Product

Time (min)	*A7*	*Marketed Product*
0	0.00	0.00
5	55.47	53.54
10	75.80	73.70
15	86.30	86.90
20	88.95	89.90
25	92.58	93.60
30	99.80	98.99

Table 9: Information regarding assessments of the physical appearance following stability investigations of MDT (Multi-Unit Tablet) in batch "A7.

Time(min)	*Color*	*Odor*
Tablets of zero days	snowy	odorless
Tablets of 15th day	snowy	odorless
Tablets of one month	snowy	odorless

Formulation Batches (Pre-compression parameter)

The data of assessment of powder blends as well as formulation batches in formulation batches A1 to A7 will be given in Table 3 and 4, respectively.

Post compression parameter

Dissolution report for the batches A1 to A7: *in-vitro* Drug release studies in Table 5 and Figure 3.

Optimization of the best batch

The assessment was conducted on the formulations to determine their characteristics or properties like friability, hardness, wet time, weight variation and dissolution time. The data given in Table 6.

Every formulation show satisfactory characteristics or properties and complies with the in-house condition for hardness, weight variation and friability, dissolution time, %CDR.

Table 6: Result of evaluation of tablets of Formulation batch A7

Formulation batches	*Dissolution time (sec)*	*Friability (%)*	*Wet time (sec)*	*Hardness (kg/cm^3)*	*Weight variation (mg)*	*%CDR*
A7	17 ± 0.524	0.231 ± 0.057	11 ± 0.212	3.26 ± 0.057	100 ± 1.77	99.80

Table 10: Data for evaluation of physical appearance and property after 1 month studies of MDT in Batch "A7"

Time	*Disintegration time (sec)*	*Friability (%)*	*Wetting time (sec)*	*Hardness (kg/cm^3)*	*Weight variation (mg)*
Zero day	17 ± 0.524	0.231 ± 0.057	11 ± 0.212	3.26 ± 0.05	100 ± 1.77
After 15th day	15 ± 0.42	0.20 ± 0.047	9 ± 0.20	3.01 ± 0.03	98 ± 1.86
After one month	16 ± 0.50	0.22 ± 0.561	8 ± 0.11	3.12 ± 0.02	101 ± 1.87

Table 11: Release of biperiden HCL from batch A7 on day zero, samples at 15 days, and post-one-month stability studies of batch A7.

Time(min)	*Zero day*	*15 day*	*One month*
0	0.00	0.00	0.00
5	55.47	53.80	54.50
10	75.80	73.15	75.30
15	86.30	82.50	84.50
20	88.95	85.95	85.90
25	92.58	90.95	89.80
30	99.80	96.96	97.85

Comparison with the marketed product

For evaluation, conventional formulations were employed and exposed to the assessment of characteristics, counting the examination of API release patterns. The outcomes for the characteristics are presented in below Table 7, while the data concerning the API release prototype are detailed in Table 8.

Brand name

Akineton Labelled claim: 2 mg Biperiden HCl

It can be inferred that tablets from formulation 'B7' exhibited a drug release of 55.47% within 15 minutes. In comparison, the marketed product demonstrated approximately 53.54% simultaneous and almost identical drug release 99.80% release of the drug in a time span of 30 minutes. These consequences suggest that the ready batch have the potential to enhance solubility.

Stability study of optimized batch

The stability of an API is distinct as the formulation's capability, within a proper packing, to maintain its characteristics or properties. Mouth dissolving batch A7 tablet is underwent an accelerated stability study at 40 ± 2ºC and 75 ± 5% RH around 1 month in an appropriate suitable stability chamber. sample were examined After 1 month for any alterations in its characteristics or properties. The surfaces exhibited no changes in color, appearance, or the presence of spots. Additionally, no indications of microbial alterations, fungal proliferation, or unpleasant odor were observed. The tablets maintained their softness, and subsequent analyses were conducted on physical appearance, solidity, disintegration time, and dissolution drug release studies. The results obtained are tabulated in Table 9.[18,19]

In Table 10 each data point represents the mean of three measurements.

In Table 11 each data point represents the mean of three measurements.

Upon comparison, noted that there were no alterations in the outer characteristics and medicine release profiles of tablets from batches 'A7' after a one-month storage period. The tablets maintained a consistent drug release pattern during this time.

CONCLUSION

An effective analytical method utilizing UV-visible spectrophotometry was devised for biperiden hydrochloride, identifying the λ_{Max} at 259 nm in a suitable buffer solution with an appropriate pH of 6.8. FTIR spectra confirmed that biperiden hydrochloride did not interfere with the excipients employed. Procedures for manufacturing mouth-dissolving tablets through direct compression were established, and successful preparation of these tablets was achieved. The formulations were based on super disintegration, incorporating different concentrations of the super disintegrant and specifically utilizing sodium starch glycolate (5.5%) through the direct compression method. The tablets underwent thorough evaluation, encompassing pharmacopoeia and non-pharmacopoeia (industry-specified) tests.

Among all the developed formulations for mouth-dissolving tablets, 'A7' was identified as the superior formulation based on the obtained results. The liberation of biperiden HCL from the tablets demonstrated a direct correlation with the concentration of the superdisintegrant used. In laboratory studies exposed that the optimized formulations achieved almost 99.80% release of the drug in less than half an hour, with an *in-vitro* dissolution time of 17 seconds, surpassing the drug release profile of the marketed product, which was found to be 98.50% within the same time frame.

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