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Research Article

FORMULATION DEVELOPMENT STUDIES ON GASTRORETENTIVE FLOATING DRUG DELIVERY SYSTEM OF FORSKOLIN-A NATURAL ROOT EXTRACT OF COLEUS FORSKOHLII

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ABSTRACT

In the present study, Forskolin, a natural root extract from the Coleus Forskohlii, was developed into a gastro retentive floating drug delivery system, using different grades of HPMC. The drug is used as anti-obesity agent reducing fat in body muscles. Forskolin increases cAMP accumulation, and therefore stimulates lipolysis. So, with high concentrations of forskolin, cAMP and lipolysis increases Enhanced lipolysis increases fat degradation and fat usage as a fuel in the body. This may promote fat and weight loss. It is thought that supplementing with forskolin may enhance fat loss without loss of muscle mass .Presently the drug is available in conventional capsule dosage form with effect on systolic blood pressure. In floating drug delivery ,the release rate of drug was controlled minimizing dose related side effects. The cumulative drug release was fitted in different kinetic models and statistically validated.

Key Words: Forskolin, Coleus Forskohlii ,cAMP, HPMC, Floating Tablet ,Higuchi Kinetics

INTRODUCTION

Coleus plants, a naturally occurring tuber crop, are durable and easy to grow. They are best known for their bright colours, and variety of foliage forms. Although they are technically a "tender perennial" (even the slightest frost will cause them to die), they are most often considered to be an annual plant by growers and seed producers. In traditional Asian systems of medicine, Coleus is used for a variety of purposes, including treating skin rashes, asthma, bronchitis, insomnia, epilepsy and angina. Coleus Forskohlii Extract is an ayurvedic herb. It has been identified as the primary chemical of interest in the plant. Forskolin activates an enzyme cells known as adenylatecyclase. This enzyme increases the level of cyclic AMP which is the most important cell regulating compound in the body.

An increased level of cyclic AMP improves circulation, decreases histamine releases and allergic compounds, improves the contraction of heat muscle, relaxes arteries which promote normal blood pressure, increases insulin secretion which in turn supports normal sugar levels in the blood, promotes relaxation of bronchial muscles promoting normal breathing and lastly supports improved fat breakdown. It has been demonstrated that adipose tissue metabolism varies from one region of the body to another, for example, in severely obese women losing weight after the jejuno-ileal bypass surgery, fat was seen to be absorbed more slowly in the thigh region than the abdominal region. These differences lead to the hypothesis that localized application of agents that trigger lipolysis or fat breakdown could help in cases of fat accumulation at specific subcutaneous sites. Forskolin accelerates lipolysis through the activation of hormone-sensitive lipase.In the gastro retentive floating drug delivery system the drug showed a uniform controlled release upto nine hours following Higuchi kinetics and release was also statistically validated.

Materials and Methods

Table 1: List of drug and polymers used for the preparation of Gastro retentive Floating Tablet Of Forskolin

1.	Forskolin	Purchased from Lakshya Herbs(Pvt)Ltd, UP
2.	HPMC different grades	LobaChemie , Mumbai,
3.	Citric Acid	E Merck , Germany
4.	Sodium Bi Carbonate	Purchased locally
5.	PVP K-30	LobaChemie, Mumbai
6.	Isopropyl Alcohal	E Merck , Germany

Preparation of Pure Forskolin from dried roots of Coleus Forskohlii

A simple, safe, rapid and economical method was developed for the isolation of high-purity Forskolin from Coleus forskohlii roots using activated charcoal as an adsorbent in a column. The elution was carried out under reduced pressure to make the process rapid. Activated charcoal acted as a reversed phase adsorbent and allowed elution of forskolin without much impurities. The residue, obtained from the elute was purified and crystallized using different solvent mixtures to obtain pure forskolin. The Forskolin isolated was analyzed and characterized by UV, IR, RP-HPLC, electro spray ionization MS, H NMR and C NMR. The yield was 0.097% w/w (RSD 5.6%). The purity was 96.9% w/w (RSD 0.3%) as determined by RP-HPLC.

Table 2: Pre Formulation Study Of Forskolin

Description	White crystalline powder
Solubility	Soluble in Chloroform, benzene, methanol, dichloromethane, sparingly soluble in petroleum ether.
Identification (by Spectroscopy & Chromatography)	
FTIR Identical with reference standard	
MASS SPECTRUM Characteristic of Forskolin	
TLC & HPTLC Gives single spot	
HPLC Retention time matches with the reference standard	
Loss on drying at 105^{o}C< 1%w/w	
Melting range223^{0} - 232^{o}c	
Purity (Forskolin content)> 97%w/w	

Table 3: Anova study

Absorption maximum	286 nm
Beer law limit	50-100mcg/ml
Correlation coefficient (r)	0.9987
r squired	0.999
regression equation	Y=0.003x+0.025
p value	<0.0001(extremely significant)
standard deviation	0.0671
linear regression	0.2761
deviation from linearity	0.00217

Preparation of Floating Tablets Of Forskolin

The Ingredients were weighed accurately and mixed thoroughly. Granulation was done with a solution of PVP K-30 in sufficient isopropyl alcohol. The granules (40mesh)were dried in conventional hot air oven at 45^{0}C.Drying of the granules was stopped when the sample taken from the oven reached a loss on drying value of 1-3%

as measured by a moisture balance at 105^{0}C.The dried granules were sized through40/60 mesh, ,lubricated with magnesium stearate(0.5%w/w)and purified talc(0.5%w/w)and then compressed on a single punch tablet machine(Cadmach Machinery Limited, Ahmedabad,India).The tablets were round and flat with an average diameter of 6mm.

In Vitro Drug Release Study

The release of Forskolin from the floating tablet to the surrounding sink solution was carried out at pH 1.2 phosphate buffer media9 as per USP dissolution apparatus. The concentration of Forskolin was determined spectrophotometrically at λ_{max}286nm in three batches F1, F2, F3 containing different grades of HPMC namelyK100,C50 andC5.Cumulative % of drug release was calculated using an equation obtained from standard curve.

RESULTS AND DISCUSSION

Process variables and optimization chart for Forskolin Floating Tablet.

Table 4: Composition of Floating Tablets of Forskolin

Ingredients (mg per tablet)	F1	F2	F3
Forskolin	20	20	20
HPMC C5	35	-	-
HPMC C50	-	35	-
HPMC K100	-	-	35
Citric Acid	15	15	15
Sodium bicarbonate	40	40	40
PVP K30	4	4	10

Table 5: Flow properties of Granules

Code	Angle of repose	Bulk Density(g/cm^2)	Tapped Density(g/cm^2)	Hausner ratio (H_R)	Carr Index (I_c)
F1	26.528±0.235^o	0.574±0.058	0.652±0.083	1.135	.0.136
F2	24,512±0.290^0	0.567±0.045	0.674±0.061	1.188	0.119
F3	28.462±0.850^o	0.582±0.029	0.667±0.052	1.146	0.154

Table 6: Physico Chemical Characterization of Floating Tablet

Code	Uniformity of weight (mg)	Hardness (kg/cm^2)	Friability (%)	Drug content (mg)	Floating lag time (s)	Total floating Time (h)
F1	110±0.25	5.25±0.11	0.54±0.09	20.25±0.15	34.01±1.65	6.12±0.03
F2	109.9±0.20	6.00±0.07	0.57±0.06	20.23±0.35	39.02±2.40	6.75±0.05
F3	110.4±0.29	5.75±0.19	0.68±0.07	20.24±0.12	71.57±1.15	12.25±0.06

Table 7:Comparitive Study of Drug Release In Zero Order Kinetics.

Formulation code	TIME									
	T0	T1	T2	T3	T4	T5	T6	T7	T8	T9
F1	0	28.71	41.91	50.55	64.64	71.23	90.26	-	-	-
F2	0	29.72	42.93	52.66	62.45	76.23	89.54	-	-	-
F3	0	28.70	41.92	51.65	61.45	72.43	81.45	84.31	94.52	98.56

Table 8: Comparative Study of Drug Release in Higuchi Model.

Sq root of time	cum % drug release		
	F1	F2	F3
0	0	0	0
1	28.71	29.72	28.70
1.414	41.91	42.93	41.92
1.732	50.55	52.66	51.65
2.000	64.64	62.45	61.45
2.236	71.23	76.23	72.43
2.449	90.26	89.54	81.45
2.645			84.31
2.828			94.52
3.000			98.56

Table 9: Comparitive Study of Drug Release In KoresmeyerPeppas Model.

LOG TIME	log cum % drug release		
	F1	F2	F3
0	**1.4580**	**1.6223**	**1.7037**
0.3010	**1.6154**	**1.7095**	**1.7375**
0.4771	**1.7096**	**1.8211**	**1.7626**
0.6020	**1.8550**	**1.8590**	**1.7967**
0.6989	**1.9407**	**1.9306**	**1.8209**
0.7781	**1.9554**	**1.9604**	**1.8437**
0.8450			**1.9182**
0.9030			**1.9755**
0.9542			**1.9937**

Table 10: Comparative study of Kinetics of In Vitro Forskolin release from Floating tablets.

Code	Zero Order		Higuchi Model		Koresmeyer Model	
	k_0	r^2	k_1	r^2	n	r^2
F1	13.52	0.964	34.86	0.971	0.677	0.976
F2	13.61	0.965	35.21	0.975	0.447	0.980
F3	10.06	0.944	33.72	0.994	0.283	0.989

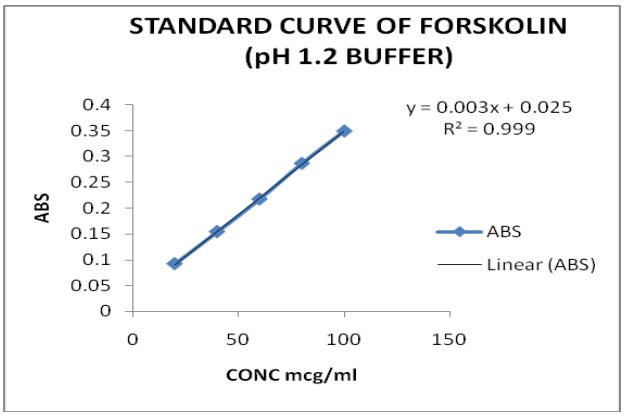

Fig 1: Standard curve of forskolin.

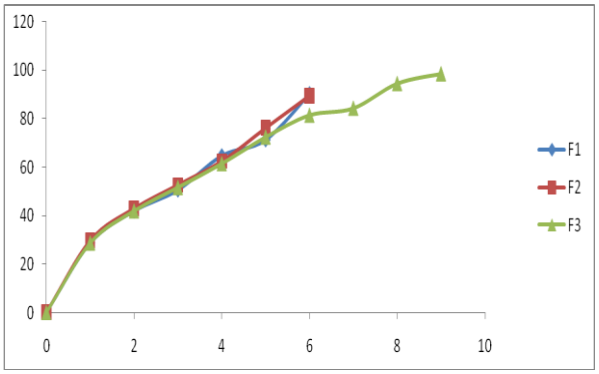

Fig 2: Cumulative % of Drug Release vs Time

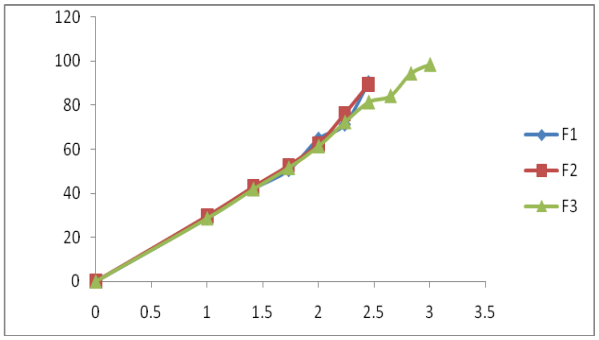

Fig 3: Higuchi Model

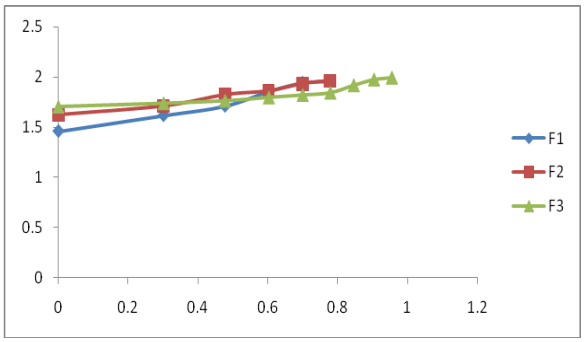

Fig 4: Koresmeyer Model

DISCUSSION

A total no of three batches namely F1, F2,F3 prepared in the form of gastro retentive floating tablet for the herbal drug Forskolin isolated and purified from roots of Coleus Forskohlii.The flow properties of the granules were found satisfactory with bulk density varying from0.567±0.045 to0.582±0.029 and angle of repose varies from24.5120to28.4620. Different grades of HPMC namely C5, C50 and K100 were used as polymer in the floating tablet formulation.The formulation containing HPMC K100 in Batch F3 showed good floating behavior to have a retention of 12hours and above.in pH1.2 buffer solution.It confirms that the drug can be successfully formulated and used as a gastro retentive floating delivery system. The release pattern of drug from the floating tablet varies from28.70% to 98.56% in acidic buffer upto nine hours supporting the good sustainable nature of the formulation.On fitting the release pattern in different kinetic model, the batch F3 showed an r^2 value of 0.994 in Higuchi Kinetics which is quite significant.

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