ISSN: 2395-0536 Impact Factor- 2.90*

INTERNATIONAL JOURNAL OF PHARMACEUTICAL RESEARCH AND NOVEL SCIENCES

IJPRNS

FORMULATION DEVELOPMENT AND INVITRO EVALUATION OF CARVEDILOL SUBLINGUAL TABLETS

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ABSTRACT

In the present work, Subligualtablets of Carvedilol were prepared by direct compression method. IR-spectroscopic studies indicated that there are no drug–excipients interactions. All the tablets were subjected to weight variation, drug content uniformity, and hardness, and friability, water absorption ratio, wetting time, dissolution, drug excipients interaction and short-term stability studies. The hardness of the prepared tablets was found to be in the range of 3.0 to 3.4 kg/ cm^2. Thefriability values were found to be in the range of 0.33 to 0.47 %.Disintegration time was found to be in the range of 1-3min. Formulation C3 showed good results than rest of the other formulations in pre and post compression studies. The average weight and drug content of the prepared tablets indicate weight and drug content uniformity within the batches prepared. Formulation C3 (101) displayed maximum drug release.

Key Words: Subligualtablets, Carvedilol

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INTRODUCTION

A solid dosage form is drug delivery system that includes tablets, capsules, sachets and pills as well as a bulk or unit-dose powders and granules. Among the various dosage forms oral soliddosage forms have greater importance and occupy a prime role in the pharmaceutical market. Oral route of drug administration is widely acceptable and drugs administered orally as solid dosage form represents the preferred class of products. Over 90% of drugs formulated to produce systemic effects are produced as solid dosage forms. Because of these reason whenever New chemical entity (NCE) has discovered, which shows a sufficient pharmacological action, first the pharmaceutical company asks whether the drug is successfully administered by oral route or not.Systemic drug delivery provide immediate onset of pharmacological effect through the sublingual route. Dysphagia (difficulty in swallowing) is a common problem of all age groups, children, elderly, uncooperative or on reduced liquid intake have difficulties in swallowing these dosage forms.1,2 Sublingual administration of the drug means placement of the drug under the tongue and drug reaches directly in to the blood stream through the ventral surface of the tongue and floor of the mouth. The drug solutes are rapidly absorbed into the reticulated vein which lies underneath the oral mucosa, and transported through the facial veins, internal jugular vein, and brachiocephalic vein and then drained in to systemic circulation. Within the oral cavity, delivery of drugs via the membranes of the oral cavity. Small to moderate molecular weight. Good stability in water and saliva. Partially no ionized

at the oral cavities pH.Under going first pass effect e.g. ketotifen fumarate. Many drug properties could potentially affect the performance of sublingual tablets like solubility, crystal morphology, particle size, hygroscopicity, compressibility and bulk density of drug. Some drugs undergoes extensive first pass metabolism which results in poor bioavailability of its oral dosage forms, that kind of drugs are suitable for sublingual dosage form. Drugs that are unstable in parenteral preparation are suitable for sublingual dosage form. Many pharmaceuticals are designed for sublingual administration, including cardiovascular drugs, steroids, barbiturates, enzymes, antiemetics, vitamins, minerals and vaccines (1-4).The aim of present work is to develop Carvedilol sublingual tablet dosage form.

MATERIALS AND METHODS

Formulation development (5-8)

The aim of the formulation development was to develop a bioequivalent product with respect to reference product with similar physical, chemical characteristics and similar stability profile. The Reference product has LHPC, Mannitol, Crospovidone, Cross Carmellose Sodium, Magnesium stearate, Sodium sachharin. From the basic literature search, excipients compatibility study and patent,underlying following excipients were selected to initiate the development work (Table-1)

Table-1 Formulation of CarvedilolSublingual Tablets

Ingredients (mg)	C1	C2	C3	C4	C5	C6	C7	C8	C9
Carvedilol (mg)	6.25	6.25	6.25	6.25	6.25	6.25	6.25	6.25	6.25
LHPC 21 (mg)	5	10	15	-	-	-	-	-	-
CP(mg)	-	-	-	5	10	15	-	-	-
CCS	-	-	-	-	-	-	5	10	15
Mg.stearate (%)	1	1	1	1	1	1	1	1	1
Aerosil (%)	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5
Mannitol	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s
Sodium sachharin	4.5	4.5	4.5	4.5	4.5	4.5	4.5	4.5	4.5
Total	200	200	200	200	200	200	200	200	200

In-Vitro Disintegration Test

The test was carried out on 6 tablets using the apparatus specified in I.P. 1996 distilled water at 37ºC ± 2ºC was used as a disintegration media and the time in second taken for complete disintegration of the tablet with no palable mass remaining in the apparatus was measured in seconds.

In-VitroDissolution

Method

Dissolution media was taken as 6.8pH phosphate buffer, 900ml.was placed in the vessel and the USP apparatus –2 (paddle) was assembled. The medium was allowed to equilibrate to temp of 37 ± 0.5°C. Tablet was placed in the vessel; the apparatus was operated at 50 rpm. At definite time intervals, 5 ml of the fluid was withdrawn; filtered and again 5ml of the fluid was replaced. The samples were analyzed using U.V.

Stability Studies

FDA and ICH specifies the guidelines for stability testing of new drug products, as a technical requirement for the registration of pharmaceuticals for human life.The ICH tripartite guidelines have established long term stability testing to be done at 25^0C/60%RH for 12 months. Accelerated stability testing should be done at 40^0 C/75%RH for 6 months and stability testing at intermediate storage conditions should be done at 30^0C/65%RH.

RESULTS AND DISCUSSION

All the formulations were evaluated for bulk density, tapped density, % compressibility, hausner's ratio and angle of repose. The results of % compressibility, hausner's ratio and angle of repose were found to be <16, <1.25 and <30 respectively. These results show that the formulations have very good flow properties (Table-2).

Table-2 Micromeritic Properties

FORMULATION	BULK DENSITY gm/ml	TAPPED DENSITY gm/ml	CARR'S INDEX %	Hausner ratio	Angle of repose
C1	0.44	0.50	12.03	1.13	24
C2	0.46	0.54	14.81	1.17	24
C3	0.66	0.77	14.28	1.16	23
C4	0.72	0.83	13.25	1.15	24
C5	0.76	0.85	11.58	1.12	24
C6	0.40	0.47	14.89	1.18	25
C7	0.70	0.83	15.66	1.19	26
C8	0.74	0.85	12.94	1.14	24
C9	0.40	0.47	14.89	1.18	25

In -vitro drug release study

Paddle method Dissolution data of Oro Dispersible formulations of Carvedilolby Paddle method (USP II) are reported in Fig-1 and 2.

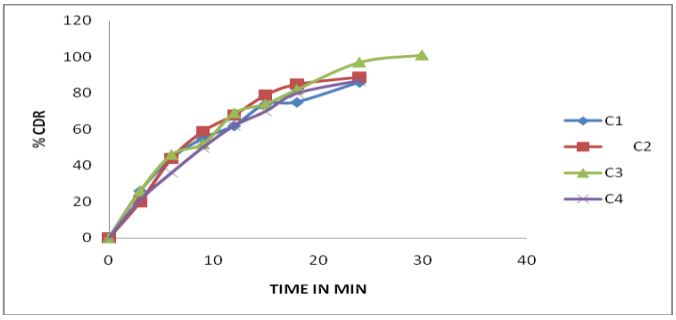

Fig-1In -vitro drug release graph for C1-C4 formulations

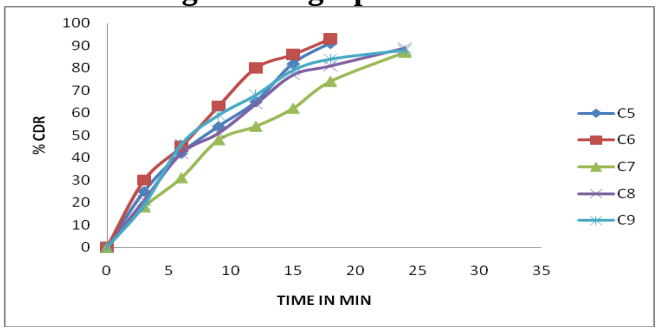

Fig-2In -vitro drug release graph for C5-C9 formulations

There was no significant change in physical and chemical properties of thetablets of formulation C-3 after 3 Months. Parameters quantified at various time intervals were shown in table-3.

Table-3 Results of stability studies of optimized formulation C-3

S.NO	Parameters	Initial	1 month	2 month	3 month	Limits as per specification
1	**40^0C/75% RH % Release**	101	100.98	99.79	99.12	**Not less than 85 %**
2	**40^0C/75% RH Assay Value**	101	100.96	99.22	99.00	**Not less than 90 % Not more than110 %**

CONCLUSION

In the present work, Subligualtablets of Carvedilol were prepared by direct compression method. All the tablets were subjected to weight variation, drug content uniformity, and hardness, and friability, water absorption ratio, wetting time, dissolution, drug excipients interaction and short-term stability studies.Tablets prepared by direct compression method were found to be good without any chipping, capping and sticking. The hardness of the prepared tablets was found to be in the range of 3.0 to 3.4 kg/ cm^2. Thefriability values were found to be in the range of 0.33 to 0.47 %.Disintegration time was found to be in the range of 1-3min.Formulation C3 showed good results than rest of the other formulations in pre and post compression studies.The average weight and drug content of the prepared tablets indicate weight and drug content uniformity within the batches prepared. Formulation C3 (101) displayed maximum drug release.IR-spectroscopic studies indicated that there are no drug–excipients interactions.

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