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Research Article

FORMULATION AND IN-VITRO EVALUATION OF EFFERVESCENT TABLETS OF AMLODIPINE

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Abstract

Hypertension is the commonest cause of high blood pressure in the elderly. The incidence increases with age advancement. Long acting dihydropyridines like amlodipine is very effective antihypertensive agent in management of ISH in elderly because of its vasodilatory as well as negative inotropic effect. The main Aim of Present work is to Formulate and Evaluate Amlodipine besylate Effervescent and direct compression tablets in order to enhance its Bio-availability by using Amlodipine besylate are the main ingredients in effervescent Tablets and Fast Disintegrating agents like sodium starch glycolate, Cross coramilose. Different batches of (F1-F6) immediate release tablets of Amlodipine besylate were prepared by using various concentrations of Citric acid & Sodium bicarbonate as effervescent agents and sodium starch glycolate, Cross cormilose as super disintegrates. Evaluation parameters like thickness, hardness, friability, weight variation and disintegration tests of the formulations were found to be satisfactory. Among all prepared formulations F6 was shown desired release pattern than others. Formulations F1- F6 did not show the optimum drug release .Hence effervescent technique is superior to direct compression by super disintegrates. And thus the F6 formulation was found to be the desired immediate release tablet for the treatment of Hypertension

Key words: Amlodipine besylate, Citric acid , Sodium bicarbonate ,sodium starch glycolate, and Cross carmilose

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INTRODUCTION

Floating drug delivery systems were first described by Davis in 1968[1,2]. It is possible to prolong the gastric residence time of drugs using these systems. Several techniques were used to design gastro retentive dosage forms. These include, floating drug delivery systems (FDDS), high-density DDS, muco-adhesive systems, swelling and expanding DDS, modified shape systems, and other delayed gastric devices[3,4]. Floating drug delivery systems, also called as hydrodynamically balanced system, is an effective technology to prolong the gastric residence time in order to improve the bioavailability of the drug[5]. This technology is suitable for drugs with an absorption window in the stomach or in the upper part of small intestine[6], drugs acting locally in the stomach[7] and for the drugs that are poorly soluble or unstable in the intestinal fluid[8]. Effervescent floating drug delivery systems generate gas (Co₂), thus reduce the density of the system and remain buoyant in the stomach for a prolonged period of time and released the drug slowly at a desired rate[9,10,11].

Amlodipine is long acting calcium channel blocker and used in the treatment of hypertension, and chronic stable angina. In hypertension or angina, initially 5 mg. one daily and adjusted to maximum dose 10 mg one daily dose of Amlodipine is given orally[12]. Amlodipine has maximum solubility in acidic pH. Amlodipine has some adverse effect such as nausea, abdominal pain. Effervescent floating tablet of Amlodipine besylate retain in stomach improves solubility, bioavailability, reduces drug waste and decrease side effect such as gastric

irritation and nausea[13]. In present work, effervescent floating tablets of different formulation were developed with an objective of achieving maximum

floating and drug release time

MATERIALS AND METHOD:

Materials:

Amlodipine Besilate was procured from Dr.Reddys Laboratories, Hyderabad. Citric Acid, Sodium Bicarbonate, Sodium starch glycolate, Croscarmellose, Mannitol, Magnesium Stearate, Talc were obtained from Colorcon Asia Pvt. Ltd and Loba chemicals.

Preparation of Amlodipine besylate Fast dissolving tablets:

The Amlodipine besylate effervescent tablets were formulated and evaluated by using different drug pure Amlodipine besylate and excipients like Citric acid, Sodium Bicarbonate, Sodium starch glycolate, Croscarmellose, Magesium stearate, Talc. By using the above ingredients the Amlodipine besylate effervescent tablets were prepared. Different formulations F1, F2, F3, F4, F5 and F6 were prepared and their composition was showed in the table 1. After the mixing of all ingredients in direct compression, they are compressed to get final product. The compression is done either by single punch machine (stamping press) or by multi station machine (rotary press). The tablet press is a high-speed mechanical device. It 'squeezes' the ingredients into the required tablet shape with extreme precision. It can make the tablet in many shapes, although they are usually round or oval.

Table 1: Composition of Amlodipine besylate Effervescent Tablet 100mg

S. No	Name of ingredients	F1	F2	F3	F4	F5	F6
1.	Amlodipine Besylate (mg)	10	10	10	10	10	10
2.	Sodium starch glycolate (mg)	4	6	-	-	-	-
3.	Croscarmellose (mg)	-	-	4	6	-	-
4.	Citric Acid (mg)	-	-	-	-	20	40
5.	Sodium Bicarbonate (mg)	-	-	-	-	40	20
6.	Mannitol (mg)	81	79	81	79	25	25
7.	Magnesium Stearate (mg)	3	3	3	3	3	3
8.	Talc (mg)	2	2	2	2	2	2

Pre formulation Studies

The general preformulation tests for the tablet formulations include the following:

Bulk density: Bulk density is defined as the mass of the powder divided by the bulk volume. The bulk density (gm/cm^3) of powder depends mainly on particle-size distribution, particle shape, and then tendency of the particles to adhere to one another.

It is given by following equation

$$D = M / V$$

Where,

D – Bulk density

M- Mass of the particles

V – Bulk volume

Compressibility Index: The initial & final density's can be used to determine the percentage compressibility also called as compressibility index.

It is given by the equation:

$$I = (D_1 - D_0 / D_1) * 100$$

Where,

I – Compressibility index

D_1 – Final density

D_0 – Initial density

The compressibility of a powder dictates its flow properties. A highly compressible powder exhibits less flow properties and vice-versa.

Angle of repose: Angle of repose is defined as the maximum angle formed between the sides of the powder heap with the horizontal surface. It is a very simple technique which determines the flow properties of the powder. The equation is given as:

$$\tan \theta = H/R$$

Where,

θ - Angle of repose

R - Radius of powder bed

H -Height

Post Compressional parameters:

Hardness: The hardness of the tablet is also termed as its crushing strength. It may be defined as the compression force required break/fracture the tablet when such force is applied diametrically. The hardness of the tablet is related to its disintegration and has more pivotal role in controlling the rate of drug release from the tablet.

The hardness of the tablet formulations (F1-F6) are tested by using the Monsanto hardness tester method.

Friability: Friability in addition to hardness gives the measure of tablet strength. The friability of a tablet may be defined as its resistance to shock and abrasion encountered during the process of manufacture etc. The friability of the tablet formulations (F1-F6) are determined by using the Roche friabilator.

Weight variation test: The weight variation test is determined by individually weighing 20 tablets. In this method 20 tablets are randomly selected and weighed individually. The average weight of these

tablets is determined. The weight variation of the individual tablets is determined with respect to average weight and %weight variation. If two tablets fall out of the permissible %weight variation and none of the tablet was twice the %weight variation value, then the batch passes the weight variation test.

Disintegration test: It is a method to evaluate the rate of disintegration of solid dosage forms (tablets). Disintegration is defined as the break down of solid dosage forms into small particles after it is ingested. The disintegration test for the formulations (F1-F6) is performed in the SECOR (Scientific engineering corporation, Delhi) India disintegration test apparatus.

In Vitro Dissolution test: The dissolution test for the formulations (F1-F6) is performed in the SECOR (Scientific engineering corporation, Delhi) India dissolution test apparatus. The in-vitro release of Metformin hydrochloride from formulated tablets was carried out for 2 hours in pH 1.2 Hydro Chloric acid buffer and pH 6.8 phosphate buffer (19h). Samples were taken at 1hr, 2hr, 3hr, 5hr, 6hr, 8hr, 12hr & 19 hours and diluted to suitable concentration and analyzed for metformin hydrochloride content at 232 nm by using UV-visible spectrophotometer.

IR spectrum: The IR spectrum for the drug (metformin hydrochloride), polymers (guar gum & HPMC) and the formulated tablet was performed to identify any incompatibility between the drug and the polymers.

RESULTS AND DISCUSSIONS

Amlodipine is a potent drug for the treatment of angina, hypertension and also suitable in the treatment diabetic hypertension. Amlodipine had maximum solubility in acidic pH. Amlodipine has some adverse effect such as headache, nausea, abdominal pain.

Effervescence production, decrease the several local GIT side effect, such as gastric irritation, nausea and gastritis. The effervescent tablets of Amlodipine besylate were formulated in six different batches F1 to F6 with effervescing agent sodium bicarbonate and citric acid.

All the formulations were prepared by direct compression method. The amlodipine besylate Effervescent tablets were prepared and evaluated. We have done different types of tests for the tablets. The tests include preformulation studies and different evaluation studies. These tests are important for the determination of the properties and the quality of the formulations. The preformulation studies include Bulk density, True density, Angle of Repose and Carr's Index results were shown in table-2. The measured hardness of tablets of each formulation ranged between 2.5 to 4 kg/cm². The % friability was less than 0% to 1% in all the formulations ensuring

that the tablets were mechanically stable. All the tablets passed weight variation test as the % weight variation was within the Pharmacopoeial limits of $\pm 5\%$ of the weight. The results are shown table-3. The graph shows the FTIR spectra of Amlodipine besylate Effervescent tablets. There were no interaction between the drug and other excipients shown in figure-1.

The amlodipine besylate was having the good powder characters and in the pharmacopoeial limits. The preformulation results shows that the taken drug can be suitable for the formulations. By the above result s we can say that, the formulation F6 shows the good bioavailability. It shows 99.8 % bio- availability. These Formulations were prepared by using 10 mg Amlodipine and changing the excipients and their concentrations. The amount of the excipients was

changed for every formulation. By this the above results was obtained. In them the formulation F6 shows 99.8% bioavailability.

Comparison study with marketed product of Amlodipine besylate 10mg (Amlodipine 10) showed that the optimized formulation F6 has better control over release rate in comparison to the commercial product. The marketed product released the drug 98.3% in 12 hours whereas the optimized formulation F6 released the drug 98.3% in 12hrs. And the optimized formulation F6 give the maximum released 98.6 at 24th hours. It is, thus concluded that effervescent tablet containing Amlodipine besylate (F6 formulation) gave fast and complete drug release spread over 24 hours shown in table-4 and figure-2.

Table-2 Preformulation Parameters

S.No	Parameter	Values
1.	Bulk Density	0.58 g/ml
2.	True Density	0.49 g/ml
3.	Angle of Repose	30
4.	Carr's Index	16

Table-3: Table showing Weight variation, Hardness, Friability, Disintegration time, Dissolution

Sl. No	Formulation	Weight Variation	Hardness (Kg/Cm ²)	Friability (%)	Disintegration Time (Sec)	Assay (%)
1.	F1	Pass	2.5	0	90	93.9
2.	F2	Pass	2.5	1	80	94.9
3.	F3	Pass	2.8	1	80	95.8
4.	F4	Pass	2.5	2	90	96.12
5.	F5	Pass	3.0	1	85	98.1
6.	F6	Pass	3.2	1	75	99.8

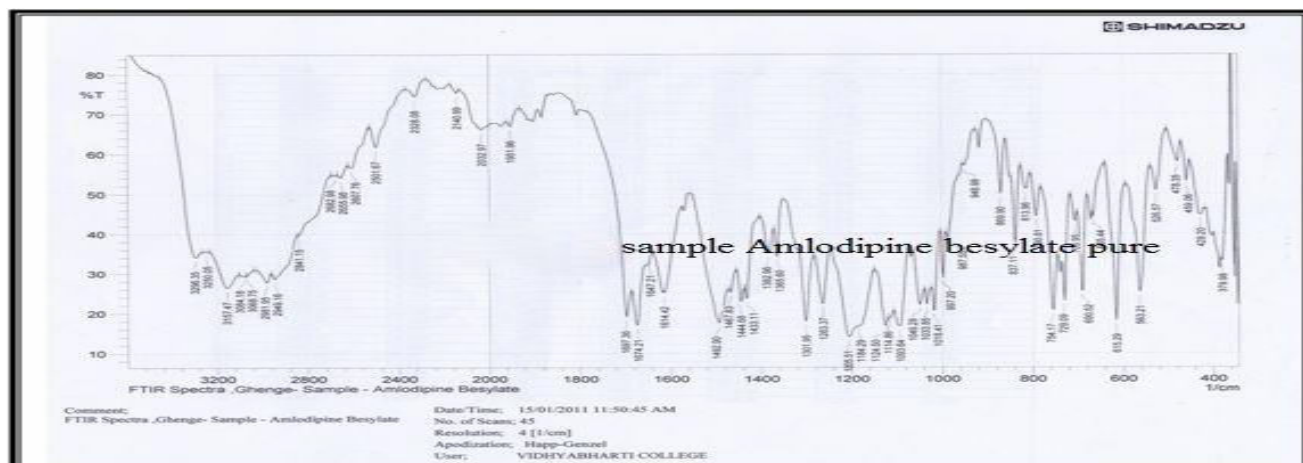


Figure- 1 FTIR Spectra of Amlodipine

Table- 4: In vitro release of Amlodipine besylate:

S. No	Time	F1	F2	F3	F4	F5	F6
1.	0	0	0	0	0	0	0
2.	5	38.6	40.2	41.5	43.2	48.1	52.2
3.	10	48.9	49.6	47.8	51.5	53.8	59.8
4.	15	57.91	58.8	61.83	63.9	65.2	67.9
5.	20	63.8	64.23	66.8	68.7	71.5	73.8
6.	25	73.15	74.1	76.2	78.8	81.5	83.8
7.	30	93.9	94.9	95.8	96.12	98.1	99.8

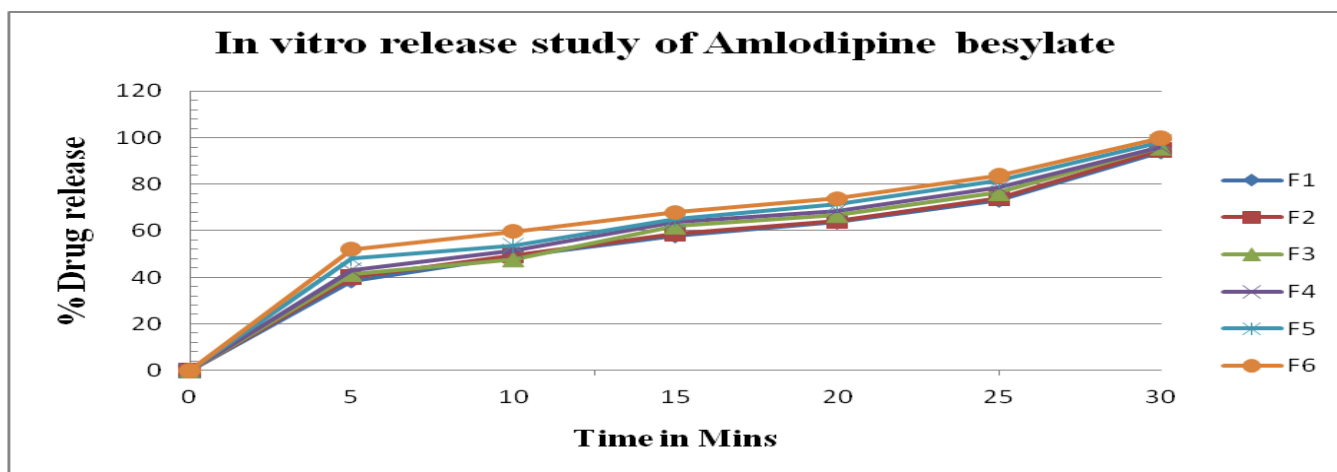


Figure-2 In vitro release study of Amlodipine besylate

CONCLUSION:

Metformin Hcl is anti hyperglycemic agent, metformin is absorbed mainly from the small intestine. Sustained release tablets of Metformin Hcl were prepared using guar gum and HPMC as retardant polymers. Various evaluation parameters like thickness, hardness, friability, weight variation and disintegration tests of the formulations were found to be satisfactory. Among all formulations prepared and evaluated F3 appeared to have desired release pattern than others. Formulations F1 and F2 did not show the optimum drug release which might be due to low level of the polymer in the tablets. Where F4 shows high drug retarding due to more concentration of polymer which could affect the drug release

Finally the F3 batch was considered as formulation extending maximum of drug release at the end of 19hrs. And thus the F3 formulation was found to be the desired sustained release matrix tablet for the treatment of type-2 diabetes mellitus.

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