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Development and Evaluation of an *In-Situ* Gelling Liquid Dosage form of an Anti- Hypertensive Drug

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Abstract

➢ ***Aim:***

This study comprises the development and evaluation of an *in-situ* gelling liquid dosage form of an anti-hypertensive drug. The anti-hypertensive drug used is Amlodipine Besylate (ADB) a long acting calcium channel blocker used for the management of angina and hypertension; the life-threatening conditions require immediate relief.

➢ ***Materials and Methods:***

Identification, authentication and compatibility of the drug and excipients were performed using Fourier Transform Infra-red (FTIR) spectroscopy and Differential Scanning Calorimetry (DSC) analysis. Sixteen formulations as per 2^4 factorial method were developed and evaluated for physical appearance, viscosity, pH, gelling time, Gelling temperature, homogeneity, clarity, Gel strength, buoyancy studies, drug content, and *in-vitro* drug release.

➢ ***Result:***

The effect of two independent factors namely concentration of gelling agent (Na Alginate) and effervescing agent calcium carbonate on various evaluation parameters were considered for the optimization of the dosage form. During evaluation studies it was found that the formulation no. GL 06 containing % of sodium alginate and 1 % of calcium carbonate shows better performance and was selected as optimised formulation.

➢ ***Conclusion:***

The effect of calcium carbonate on the gelling efficacy of various concentration of sodium alginate was studied and it was concluded that the effective gelling and drug release was achieved in the formulation comprised of 1.0 % sodium alginate with 1.0 % calcium carbonate.

Keywords:- *Amlodipine Besylate, Gastric Retention, Anti-hypertensive, Calcium Channel Blocker, Sodium Alginate, Optimization.*

I. INTRODUCTION

Amlodipine Besylate (ADB) is a calcium channel blocker, used for the management of Coronary artery diseases and in mild to moderate essential hypertension [1, 2]. The prolonged half-life, high distribution rate and slow elimination rate differentiate ADB from other drugs of this category. Amlodipine besylate (ADB) shows slow absorption when administered orally as the rate of absorption is often controlled by the rate of dissolution of the dosage form [3, 4, 5]. Various salts of amlodipine (AD) have been prepared, such as besylate, mesylate, maleate, etc. Amongst all the salts available besylate, have better solubility than AD alone [6, 7]. Countless approaches have been made to enhance the bioavailability of AD by developing new formulations, along with use of different excipients and formulation techniques, etc.[8]. In this research efforts have been made to develop an *in-situ* gelling liquid of ADB for local drug delivery to enhance the bioavailability of the drug.

The Gastric Retention Time (GRT) and Gastric Emptying Time (GET) are the unpredictable physiological challenges in the development of oral drug delivery systems [9]. It is always preferred to develop ideal drug delivery systems that will be a single dose for the duration of treatment and deliver the drug directly at the site of action. The bioavailability of drugs with narrow absorption window in stomach can be enhanced by reducing the dose. In current scenario the Gastro-retentive Drug Delivery System (GRDDS) are growing and popularising in the arena of oral drug delivery.

The issue of poor bioavailability associated with conventional oral delivery can be challenged by a simple approach of retaining the dosage form in the stomach for an extended period of time and release the drug slowly. Diverse innovative approaches like coating, pulsing cap, magnetic field assisted gastro-retention, spensules, plug type swelling system, mucco-adhesion technique, floating system are being employed to address the issue.

Less gastric retention period due to rapid empting of stomach are factor that influences the bioavailability, frequency of dose administration and dose size etc.in case of conventional oral dosage forms. To address this problem numerous efforts have been made to prolong the retention time of drug delivery system.

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Sodium alginate is a commonly used additive in pharmaceutical formulations such as beads, matrix tablets and microcapsules etc. due its broad properties. Sodium alginate undergoes gelation in the presence of di- and trivalent metal ions, dilute solutions by a process involving consecutive guluronic residues in the guluronic acid (G) blocks of the alginate chain.[10] In current research work a gelling liquid dosage form is developed to address and overcome the challenges in achieving efficient drug delivery.

II. MATERIALS AND METHODS

A. Materials

ADB (99%) was procured from Amsal Chem Pvt. Ltd. Bahruch, Gujarat (India)., Sodium alginate was a gift sample from Krishna Polymers, Ahmedabad, Gujurat, (India)., and all other chemicals and reagents used were of research grade.

B. Methods

➢ *Drug identification and confirmation of Purity*

The identification and the purity of drug and excipients were determined by IR spectroscopy using Fourier-Transform Infrared spectroscopy (FTIR) and Differential Scanning Calorimetry (DSC) spectral analysis.

➢ *Drug and excipients compatibility studies*

The Drug and excipients compatibility study was carried out by IR spectroscopy of the drug and excipients individually as well as in physical mixture using Fourier-Transform Infrared spectroscopy (FTIR) scanning measurement range of 600 to 4000 cm^{-1} and Differential Scanning Calorimetry (DSC) spectral analysis under nitrogen purging at scanning rate of 10°C/m, covering the temperature range of 30-360°C.

➢ *Preparation of in-situ gelling liquid:*

Sodium alginate solution in de-ionized water in concentrations ranging from 0.5 – 2.0% (w/v) were prepared by continuous stirring at 60°C. When the solution was cooled down to around 40°C, weighed amount of calcium carbonate ranging from 0.5 to 2.0 % (w/v) and 0.275 % drug so that each 5ml of gelling liquid should contain 13.86 mg of ADB (equivalent to 10 mg of Amlodipine) was added and mixed properly. The prepared ADB *in-situ* gelling liquid was packed and stored in an amber colour narrow mouth bottles for further studies [11] Table 1.

Sl No.	Formulation No.	Sodium Alginate (% w/v)	Calcium Carbonate (% w/v)	ADB (% w/v)
1	GL 01	0.5	0.5	0.275
2	GL 02	1	0.5	0.275
3	GL 03	1.5	0.5	0.275
4	GL 04	2	0.5	0.275
5	GL 05	0.5	1	0.275
6	GL 06	1	1	0.275
7	GL 07	1.5	1	0.275
8	GL 08	2	1	0.275
9	GL 09	0.5	1.5	0.275
10	GL 10	1	1.5	0.275
11	GL 11	1.5	1.5	0.275
12	GL 12	2	1.5	0.275
13	GL 13	0.5	2	0.275
14	GL 14	1	2	0.275
15	GL 15	1.5	2	0.275

Table 1:- Formulation composition

➢ *Evaluation Studies:*

physical appearance, viscosity, pH, gelling time, Gelling temperature, buoyancy studies, homogeneity, clarity, Gel strength, drug content, *in-vitro* drug release and stability studies.

➢ *Physical Appearance:*

All the formulations were observed visually for physical parameters such as appearance and colour and reported in Table 2.

➢ *Clarity:*

The clearness of all the formulations was determined by visual inspection of formulations before filling into containers and was reported in Table 2.

➢ *Homogeneity:*

All the prepared formulations were subjected to homogeneity testing by visual inspection in the storage containers. The presence and appearance of any aggregates was observed during storage period.[12] Homogeneity of all the formulations were noted and reported in Table 2.

➢ *Viscosity:*

The rheological properties of all the formulated *in situ* gelling liquid were evaluated using Brookfield viscometer DV-III Programmable with spindle no S- 94 at a speed of 100 rpm[13]. The viscosity of all the batches was determined and reported in Table 2.

➢ *Determination of pH:*

The pH of all the prepared gelling liquid formulations was determined using a digital pH meter; the pH meter was calibrated using phosphate buffers at pH 4 and pH 7 prior to use [14]. pH of all the batches was carried out and reported in Table 2.

Sl. NO.	Formulation No.	Appearance *	Clarity *	Homogeneity *	Viscosity (cP)*	pH*
1	GL 01	Light Yellow	Clear	Good	210.02 ± 0 .18	5.56 ± 0 .007
2	GL 02	Light Yellow	Clear	Good	672.23 ± 0 .23	5.56 ± 0 .006
3	GL 03	Light Yellow	Clear	Fair	734.85 ± 0 .19	6.50 ± 0 .008
4	GL 04	Light Yellow	Clear	Good	904.02 ± 0 .37	7.52 ± 0 .006
5	GL 05	Light Yellow	Clear	Good	351.32 ± 0 .29	5.88 ± 0 .004
6	GL 06	Light Yellow	Clear	Excellent	632.25 ± 0 .26	7.01 ± 0 .003
7	GL 07	Light Yellow	Clear	Fair	676.10 ± 0 .27	7.04 ± 0 .009
8	GL 08	Light Yellow	Clear	Good	728.02 ± 0 .10	6.84 ± 0 .008
9	GL 09	Light Yellow	Clear	Fair	106.03 ± 0 .13	6.48 ± 0 .006
10	GL 10	Light Yellow	Clear	Excellent	522.08 ± 0 .19	6.92 ± 0 .003
11	GL 11	Light Yellow	Clear	Good	745.01 ± 0 .18	6.29 ± 0 .005
12	GL 12	Light Yellow	Clear	Good	912.05 ± 0 .15	6.54 ± 0 .008
13	GL 13	Light Yellow	Clear	Excellent	101.03 ± 0 .18	7.52 ± 0 .008
14	GL 14	Light Yellow	Clear	Fair	135.78 ± 0 .17	6.70 ± 0 .005
15	GL 15	Light Yellow	Clear	Good	266.45 ± 0 .15	6.35 ± 0 .007
16	GL 16	Light Yellow	Clear	Good	731.02 ± 0 .13	6.49± 0 .008
*Average of six reading is taken as final reading						

Table 2:- Evaluation parameters- Appearance, Clarity, Homogeneity, viscosity and pH

➢ *Gelling Temperature*

The gelling temperature is the temperature at which the liquid converts into gel. It was determined by placing the test tube, containing sufficient quantity of the prepared solutions, in a water bath at 4 °C. The temperature of water bath was increased slowly at a constant rate of 1 °C every 2 min. The temperature at which the meniscus of the formulation would no longer move upon slanting the test tubes at 90 ° is the gelling temperature of the formulation [15]. The gelling temperature of all the formulations was noted and recorded in Table 3.

➢ *Gelling Time:*

The formulated dosage form exists as solution prior to administration, however, once it administered it convert into a gel. The sol-gel shift of the formulated *in situ* gelling liquid was evaluated by placing 2 ml of the prepared formulation to a test tube and sealed with a film; the tube was kept in a rotary water bath at 37 °C following each time setting up to 10 min [15]. Finally, the test tube was placed horizontally and observed for gelation. The Gelling Time of all the formulated batches was recorded in Table 3.

➢ *Gel strength:*

To determine the gelling strength 5g sample from each formulation was placed in a 20 ml measuring cylinder. The formulation sample was allowed to shift into the gel using thermostat at 37 °C. 3.5 g weight was placed on the surface of the gel and the time in seconds taken by weight to penetrate 0.5 cm in gel is noted [16]. The gel strength of all the batches was reported in Table 3.

➢ *Buoyancy studies:*

The time occupied by formulated *in-situ* gel to afloat on the surface of the medium (floating lag time) was noted. It is the time for which a formulation persistently drifted over the surface of the dissolution medium [17]. The buoyancy was determined and reported in Table 3.

➢ *Drug content*

One ml of each formulation was taken in 10 ml volumetric flask to which 7.5 ml of methanol was added and stirred for 1h using magnetic stirrer the final volume was made with methanol up to the mark. The prepared solution was filtered using whattman no. 40 filter paper. For further dilution again 1 ml of prepared solution was taken in to a 10 ml volumetric flask and the volume was made up by mobile phase up to the mark. The amount of ADB was determined spectrometrically at 361 nm using quartz cells1cm path length and the concentration [18, 19] was calculated using equation no.1 and reported in Table 3.

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$$\text{Concentration} = \frac{\text{Absorbance X Dilution Factor}}{\text{A (1\%, 1cm) X 1}cm}$$

Equation …….01

Sl. NO.	Formulation No.	Gelling Temperature (˚C)*	Gelling time (sec.)*	Gel Strength * (Sec.)	Buoyancy* (Sec.)	Drug Content
1	GL 01	35.24 ± 0 .33	9.18 ± 0.13	51.67 ± 0.52	231 ± 0 .23	97.45± 0.34
2	GL 02	35.39 ± 0.21	9.14 ± 0.18	53.09 ± 0.46	242 ± 0.84	101.23 ± 0.41
3	GL 03	36.21 ± 0.20	8.40 ± 0.14	54.06 ± 0.23	262 ± 0 .45	101.67 ± 0.52
4	GL 04	36.18 ± 0.20	6.05 ± 0.15	55.09 ± 0.36	285 ± 0 .23	99.07 ± 0.78
5	GL 05	37.18 ± 0 .12	4.08 ± 0.19	53.06 ± 0.23	163 ± 0 .46	101.46 ± 0.19
6	GL 06	37.62 ± 0.19	5.23 ± 0.12	56.89 ± 0.36	194 ± 0 .43	100.48 ± 0.45
7	GL 07	37.89 ± 0.14	7.01 ± 0.23	55.45 ± 0.46	224 ± 0 .15	98.87 ± 0.49
8	GL 08	37.02 ± 0.17	6.06 ± 0.18	56.13 ± 0.34	304 ± 0 .78	97.89 ± 0.62
9	GL 09	37.32 ± 0 .18	4.14 ± 0.17	52.67 ± 0.41	281 ± 0 .51	98.98 ± 0.73
10	GL 10	36.09 ± 0.21	3.56 ± 0.18	54.74 ± 0.41	247 ± 0 .45	97.87± 0.75
11	GL 11	37.01 ± 0.18	4.06 ± 0.16	55.12 ± 0.48	318 ± 0 .19	99.54± 0.39
12	GL 12	37.50 ± 0.16	4.34 ± 0.14	55.96 ± 0.54	338 ± 0 .12	100.97 ± 0.81
13	GL 13	36.02 ± 0 .12	3.24 ± 0.19	54.98 ± 0.31	291 ± 0 .33	99.36± 0.41
14	GL 14	36.09 ± 0.17	5.09 ± 0.20	55.34 ± 0.36	314 ± 0 .12	98.46± 0.26
15	GL 15	37.03 ± 0.18	5.45 ± 0.19	56.03 ± 0.42	341 ± 0 .42	101.56± 0.15
16	GL 16	37.08 ± 0.17	5.54 ± 0.17	56.67 ± 0.39	378 ± 0 .56	97.83± 0.38
* Average of six reading is taken as final reading						

Table 3:- Evaluation parameters - Gelling Temperature, Gelling Time, Gel Strength, Buoyancy and Drug Content.

➢ *In-vitro drug release*

The cumulative *in-vitro* drug release (CDR) of each formulated gelling liquid was estimated using 6 jar USP dissolution apparatus II (Paddle Method) in 900 ml of 0.1N Hydrochloric acid of pH 2.0 at a fixed temperature of 37±0.5°C.

Ten ml of *in-situ* gelling liquid formulation was taken into a petri dish of 4.5 cm internal diameter and kept in the dissolution jar. Then the dissolution medium was poured into the dissolution jar carefully without disturbing the formulation. The Dissolution apparatus is operated at a speed of 50 rpm. At each time interval, a precisely measured 5ml sample of the dissolution medium was withdrawn and replenished with equivalent amount of pre warmed (37°C) fresh dissolution medium to maintain the sink conditions. The sample were filtered through whattman no. 40 filter paper and the amount of Amlodipine was estimated spectrophotometrically at 361 nm and the drug content was determined as described in the assay section [19, 20]. The in-vitro drug release pattern of each formulation of gelling liquid was calculated and reported in Table 4 A & B.

Time (hr.)	GL 01	GL 02	GL 03	GL 04	GL 05	GL 06	GL 07	GL 08
0.25	19.25 ± 0.014	07.19 ± 0.015	06.58 ± 0.012	05.23 ± 0.010	29.21 ± 0.012	22.25 ± 0.015	06.23 ± 0.015	05.11 ± 0.019
0.5	27.36 ± 0.018	09.46 ± 0.019	07.83 ± 0.017	06.57 ± 0.014	47.09 ± 0.013	39.85 ± 0.018	07.65 ± 0.013	07.28 ± 0.012
1	34.05 ± 0.019	11.83 ± 0.012	09.02 ± 0.019	08.56 ± 0.016	63.89 ± 0.019	47.05 ± 0.019	09.82 ± 0.014	08.25 ± 0.013
2	38.97 ± 0.014	14.96 ± 0.017	12.08 ± 0.015	10.61 ± 0.014	78.56 ± 0.012	56.97 ± 0.014	11.98 ± 0.015	10.07 ± 0.011
3	42.82 ± 0.016	18.81 ± 0.016	16.24 ± 0.013	12.58 ± 0.019	83.94 ± 0.015	63.82 ± 0.016	15.85 ± 0.010	12.25 ± 0.017

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4	47.12 ± 0.015	22.84 ± 0.012	19.93 ± 0.011	14.82 ± 0.016	89.93 ± 0.011	69.12 ± 0.015	18.81 ± 0.015	14.18 ± 0.013
5	51.56 ± 0.013	28.62 ± 0.018	23.18 ± 0.013	16.23 ± 0.011	94.89 ± 0.012	75.56 ± 0.013	23.75 ± 0.012	16.95 ± 0.010
6	57.45 ± 0.023	34.58 ± 0.016	29.57 ± 0.018	19.06 ± 0.015	99.21 ± 0.016	82.45 ± 0.023	28.93 ± 0.014	19.85 ± 0.017
7	63.08 ± 0.018	46.28 ± 0.017	34.28 ± 0.012	21.86 ± 0.013		88.08 ± 0.018	34.89 ± 0.019	22.24 ± 0.011
8	68.84 ± 0.014	58.56 ± 0.015	46.18 ± 0.011	23.92 ± 0.016		94.84 ± 0.014	46.65 ± 0.013	23.74 ± 0.012
9	74.59 ± 0.025	66.28 ± 0.020	58.29 ± 0.017	26.04 ± 0.014		96.51 ± 0.025	60.04 ± 0.018	26.84 ± 0.015
10	79.82 ± 0.013	75.83 ± 0.015	63.89 ± 0.014	30.85 ± 0.010		97.53 ± 0.013	64.49 ± 0.018	31.58 ± 0.016
11	86.51 ± 0.016	83.18 ± 0.011	70.01 ± 0.010	38.01 ± 0.013		98.24 ± 0.016	71.84 ± 0.018	38.37 ± 0.014
12	93.24 ± 0.011	88.58 ± 0.013	78.54 ± 0.011	47.95 ± 0.021		99.89 ± 0.14	79.08 ± 0.017	48.59 ± 0.018

Table 4 A:- In-vitro Drug release data of Gelling liquid from GL01 to GL 08.

Time (hr.)	GL 09	GL 10	GL 11	GL 12	GL 13	GL 14	GL 15	GL 16
0.25	30.14 ± 0.018	23.58 ± 0.014	21.87 ± 0.014	06.07 ± 0.011	31.25 ± 0.012	26.15 ± 0.011	24.02 ± 0.015	19.26 ± 0.012
0.5	54.08 ± 0.011	41.58 ± 0.010	38.97 ± 0.013	07.17 ± 0.013	55.49 ± 0.010	44.14 ± 0.012	40.18 ± 0.011	39.52 ± 0.014
1	62.19 ± 0.017	59.24 ± 0.013	47.84 ± 0.015	08.74 ± 0.012	64.85 ± 0.012	60.25 ± 0.011	57.81 ± 0.016	48.21 ± 0.013
2	74.85 ± 0.013	72.08 ± 0.010	57.24 ± 0.011	11.68 ± 0.014	76.84 ± 0.018	74.10 ± 0.015	70.88 ± 0.015	56.95 ± 0.012
3	80.47 ± 0.010	79.85 ± 0.012	64.12 ± 0.017	15.45 ± 0.010	83.46 ± 0.016	81.26 ± 0.013	77.46 ± 0.010	64.51 ± 0.018
4	88.78 ± 0.013	86.24 ± 0.016	69.94 ± 0.012	19.01 ± 0.012	91.81 ± 0.012	89.47 ± 0.011	82.74 ± 0.015	69.94 ± 0.012
5	96.28 ± 0.014	90.84 ± 0.018	76.17 ± 0.018	22.85 ± 0.016	99.84 ± 0.016	93.81 ± 0.012	88.12 ± 0.016	77.04 ± 0.010
6	99.78 ± 0.012	94.81 ± 0.015	82.95 ± 0.017	28.62 ± 0.011		99.85 ± 0.010	92.26 ± 0.011	83.54 ± 0.012
7		98.17 ± 0.014	88.77 ± 0.013	33.86 ± 0.010			96.24 ± 0.018	88.24 ± 0.017
8		99.45 ± 0.012	94.32 ± 0.010	45.42 ± 0.010			99.94 ± 0.011	94.41 ± 0.011
9			96.07 ± 0.017	57.63 ± 0.012				96.02 ± 0.012
10			97.84 ± 0.011	63.10 ± 0.019				98.17 ± 0.010
11			98.71 ± 0.015	69.92 ± 0.014				98.89 ± 0.010
12			99.74 ± 0.017	74.78 ± 0.011				99.71 ± 0.011

Table 4 B:- In-vitro Drug release data of Gelling liquid from GL09 to GL 16.

III. RESULTS AND DISCUSSION

As a qualification for any formulation the pre-formulation studies was performed to identify the drug and excipients. The purity of ADB and excipients was established by FTIR spectroscopy.. The IR spectra of pure drug and excipients was compared with pure compound IR spectra ant it was found the IR spectra taken was identical to the reference standards representing that the chemicals used were pure and safe to use. Figure 1

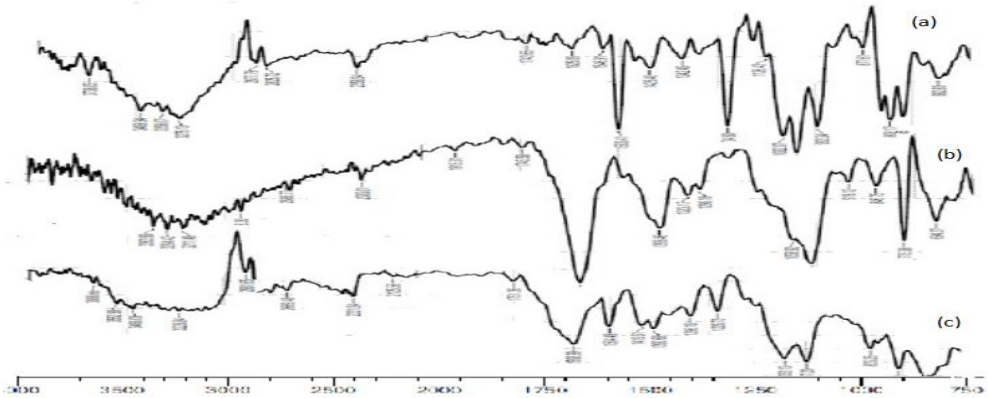

Fig 1:- IR spectra of ADB (a), Na Alginate (b) and mixture of ABD and Na Alginate (c).

The pre-formulation study reveals the purity of the drug and excipients used in this research work. The compatibility studies of the drug and excipients shows that all the major peaks for the drug and the excipients were retained in IR spectrum and no significant changes in melting point of the drug was observed in physical mixture of drug and excipients as found in DSC thermographs. The observation concludes that the drug and the excipients used are compatible. Figure 2

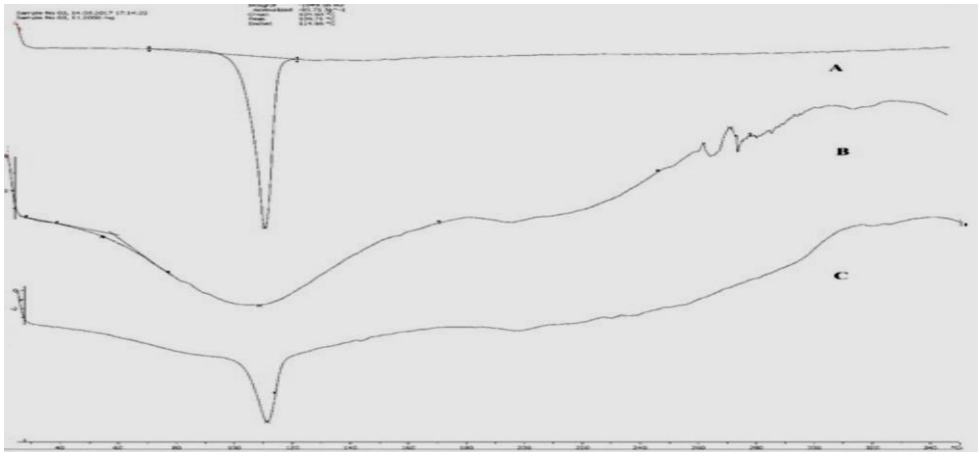

Fig 2:- DSC thermogram for ADB (A), Na Alginate (B) and Mixture of ADB & Na Alginate (C).

In this research work a total of 16 formulations of *in situ* gelling liquid of ADB was developed with different concentrations of sodium alginate and calcium carbonate. In this formulation sodium alginate is used a gelling agent and calcium carbonate as effervescing agent. The prepared gelling liquid was poured in amber colour narrow mouth glass bottles and stored in cool and dark place to protect the formulation from light and heat.

The evaluation for physical appearance, clarity and homogeneity of all the formulations was conducted visually and it was found that all the 16 formulations possess light yellow colour and are clear solutions, The homogeneity was observed after filling into the containers ad it was observed that the formulation no GL-06, GL-10 and GL-13 has shown excellent homogeneity.

The flow property of formulated gelling liquid plays an important role in pour ability and swallowing. Therefore the viscosities of the all the prepared formulations was evaluated at 100 rpm and reported in table 2. The flowability increases with the increase in sodium alginate concentration due to chain interaction with increase in polymer concentration. In other hand the flowability decreases with the increase in calcium carbonate concentration. The pH of the all the formulations did not show any irritation in the oral cavity as all the formulations pH was within in the tolerable range.

The gelling temperature of all the formulations was found in a range of 35.24 ± 0 .33 ºC and 37.89 ± 0.14 ºC, formulation no. GL-06 shows a gelling temperature of 37.62 ± 0.19 ºC which is equivalent to the temperature of stomach and ensures that the formulation will convert into

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gel as soon as it reaches the stomach. Gelling time of all the formulations was determined and was found in a range of 3.24 ± 0.19 min. and 9.14 ± 0.18 min. the gelling time of formulation no.GL 06 was found to be 5.23 ± 0.12 min. which is an ideal time for any formulation to reach the stomach and provide sufficient temperature at stomach to convert gelling liquid to gel.

The gel strength of the formulation after transformation from gelling liquid to gel was evaluated and found in the range of 51.67 ± 0.52 sec. to 56.89 ± 0.36 sec., the gel strength is the electrochemical force within the fluidic under static condition which directly affect the drug release pattern, formulation no. GL-06 represent the maximum gelling strength of 56.89 ± 0.36 which indicates the sustain release of the drug from the gel.

A perfect gastro retentive drug delivery system need least floating lag time, the buoyancy of all the prepared formulations was evaluated and it was found in the ranges from 163±0 .46 sec. to 378±0.56 sec. Formulation GL 06 which consists of 1% sodium alginate and 1 % calcium carbonate shows least floating lag time, this could be due to less concentration of calcium carbonate as the volume of gas generated was high in the formulation GL 06.

The drug content of all the formulations was determined and it was observed that the drug content was in the range of 97.45± 0.34 % to 101.89 ± 0.29 %. The results showed that all formulated gelling liquid batches have been prepared with uniformity in their content and the active drug is found to be within limit (Table 4) indicating acceptable manufacturing process.

The in-vitro drug release study was carries out and a plot of % drug release vs. time was plotted and represented Figure 4-7. The outcomes of the drug release study suggested that the formulations in which the concentration of calcium carbonate was more than or equivalent to the concentration of sodium alginate shows more than 20 % drug release in first 15 min. In other hand formulations with concentration of calcium carbonate less the concentration of sodium alginate shows drug release below 10 % in first 15 minute. The drug release pattern of formulation GL 06 represents an ideal drug release starting with 22.25± 0.015 % in first 15 minutes with 99.89± 0.14% in 12 hr. On the basis of evaluation observations formulation GL 06 was selected as optimised formulation.

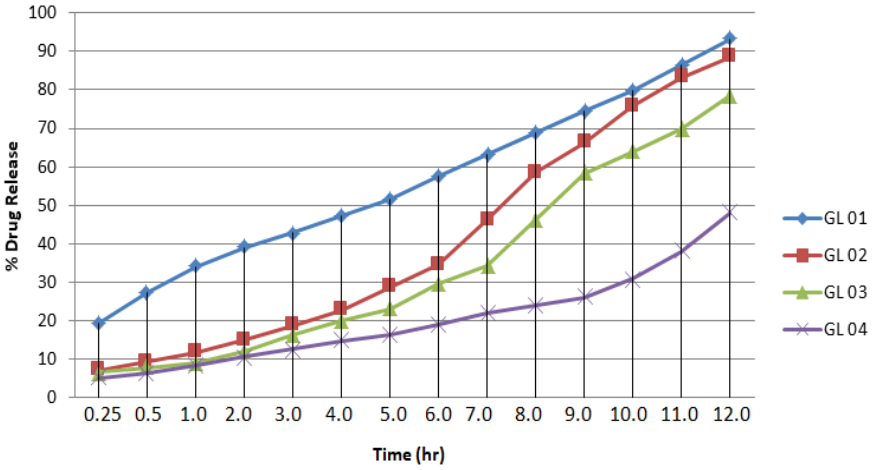

Fig 3:- In-vitro drug release from formulation GL 01, GL 02, GL 03 & GL 04

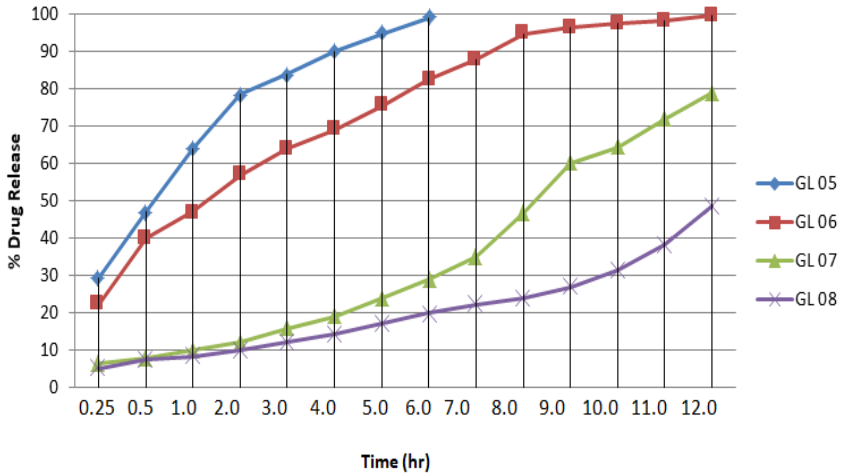

Fig 4:- In-vitro drug release from formulation GL 05, GL 06, GL 07 & GL 08

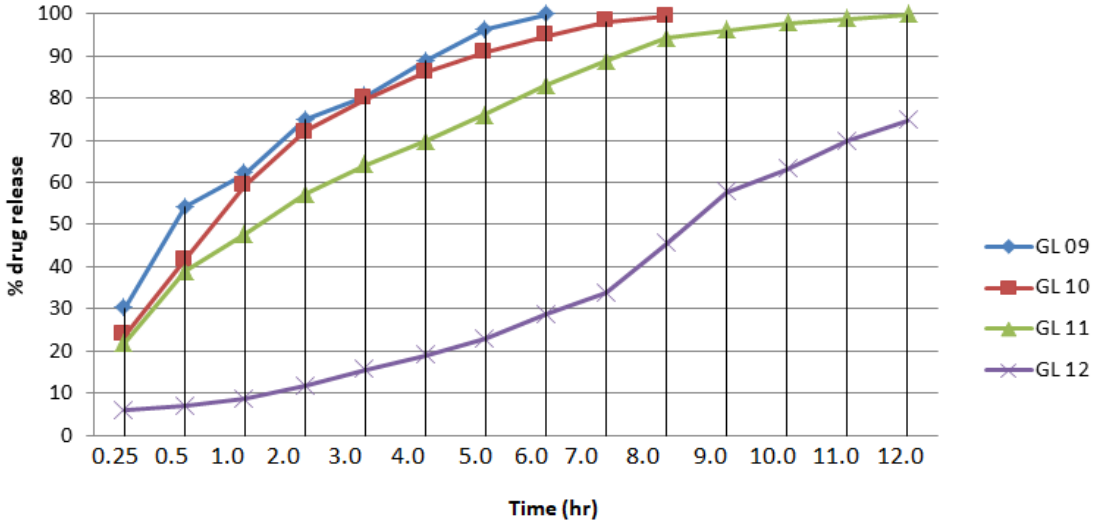

Fig 5:- In-vitro drug release from formulation GL 09, GL 10, GL 11 & GL 12

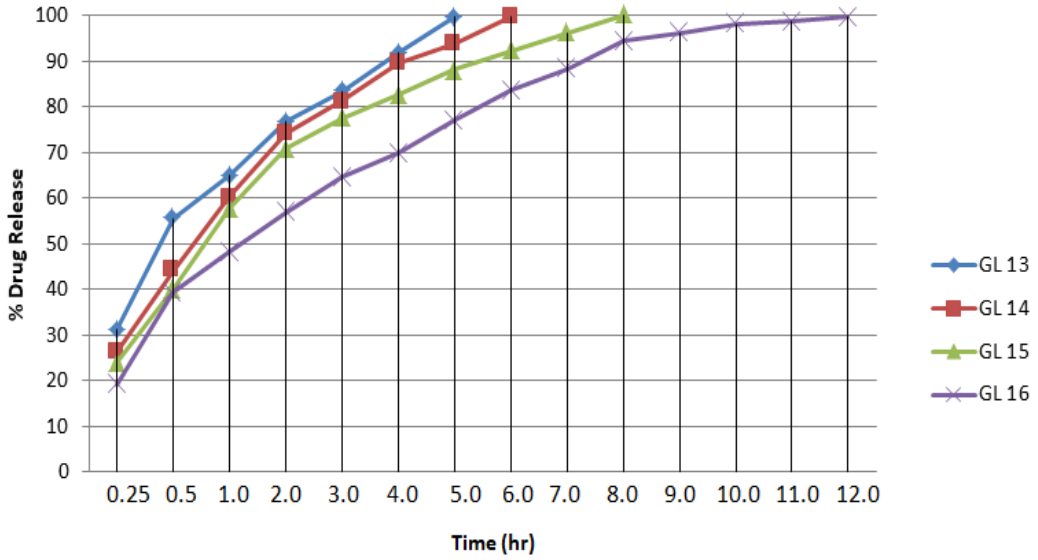

Fig 6:- In-vitro drug release from formulation GL13, GL 14, GL 15 & GL 16

Formulation GL 06 of gelling liquid Contains 1% Sodium alginate and 1 % Calcium carbonate, which was a light yellow colour clear solution with excellent homogeneity when packed in container. The viscosity of 632.25 cps, pH 7.01, gelling temperature of 37.62 ºC, gelling time 5.23 sec., gel strength of 56.89 sec., floating Lag Time of 194 sec., with a drug content of 100.48% were all the ideal parameters responsible for the selection of the formulation GL 06 as optimised formulation.

IV. CONCLUSION

The effect of calcium carbonate concentration on the gelling properties sodium alginate along with drug release from the formulations was studied in present research work and it was concluded that the effective gelling liquid was formulated with equal concentration of sodium alginate and calcium carbonate with a sustained release of drug for 24 hrs.

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