Research Article

# Immediate and Extended Release Capsule Formulation of Ajwain (*Trachyspermum ammi*) Fruit Extract

**Konda Mayuri*, Chinnala Krishna Mohan, Geggalapally Nidhi Reddy, Moola Sarika, Paladugu Sneha Reddy, Palle Annie Jerusha**
Department of Pharmaceutics, School of Pharmacy, Nalla Narasimha Reddy Education Society's Group of Institutions, Hyderabad, Telangana, India.
***Corresponding author's E-mail:** mayurikonda@gmail.com

**Received:** 15-07-2017; **Revised:** 26-08-2017; **Accepted:** 14-09-2017.

**ABSTRACT**

The kitchen ingredients have many health benefits and are used to treat disease and its symptoms. Ajwain (*Trachyspermum ammi*) is one of such element which is traditionally used as a treatment method for cough, bloating, indigestion, infections etc. from past decades. Current study enumerates the formulation and evaluation of granules prepared by wet granulation method with immediate release granules (I.R.G) and Extended release (E.R.G). The granules are evaluated for physical characteristics. The evaluated granules were filled into empty hard gelatin capsule shells with increasing quantities of I.R.G and decreasing amounts of E.R.G. Capsules were evaluated for weight variation, drug content, disintegration time and dissolution studies. The formulations were within the range of I.P limits for weight variation and disintegrated in the time limit of 14 to 17 minutes and these results are approved according to I.P (30 minutes). *In-vitro* dissolution study was conducted and the F1 showed slower release rate than other formulations due to fraction variations in filling the capsule. F7 has rapid rate of drug release due to high proportion of I.R.G. It can be concluded that Ajwain can be administered in rapid release and prolonged release dosage forms depending upon the severity of diseases.

**Keywords:** Ajwain, *Trachyspermum ammi,* SSG, HPMC, Eudragit, immediate release and extended release.

## INTRODUCTION

### Capsule

Capsule is the most adaptable of all dosage forms. Capsules are solid dosage forms in which one or more therapeutic and inert ingredients are enclosed in a small shell or container typically made of gelatin. Capsules are obtainable in many sizes to supply dosing flexibility. Disagreeable drug tastes and odors can be covered by the tasteless gelatin shell. The administration of liquid and solid drugs enclosed in hard gelatin capsules is one of the majorly utilized dosage forms[1].

### Granulation

It is the procedure of forming into grains or granules. Granules classically have a size variety between 0.2 and 4.0 mm depending on their ensuing use. Granulation is carried out for a series of reasons, one of which is to avert the segregation of the constituents of powder blend. Segregation is due to differences in the size or density of the constituent of the mix. Normally, the smaller and/or denser particles are liable to concentrate at the bottom of the container with the larger and/or less dense ones on the top. An ideal granulation will enclose all the constituents of the mix in the accurate proportion in each granule and segregation of granules wills not occur[2].

In wet granulation, granules are formed by the adding of a granulation liquid onto a powder bed which is in the influence of an impeller (in a high-shear granulator), screws (in a twin screw granulator) or air (in a fluidized bed granulator). The stir resulting in the system along with the wetting of the constituents within the formulation results in the aggregation of the primary powder particles to produce wet granules. The granulation liquid contains a solvent which ought to be volatile so that it can be removed by drying, and be non-toxic[3].

The dry granulation procedure is used to form granules without using a liquid solution because the product granulated may be responsive to moisture and heat. Forming granules without wetness requires compacting and densifying the powders. In this course the primary powder particles are aggregated under elevated pressure[4].

### Immediate Drug Release Formulation

Super-disintegrants are a driving force added to tablet and several encapsulated formulations to endorse the breakup of the tablet and capsule "slugs' into smaller remains in an aqueous environment there by increasing the obtainable surface area and promoting anadditional rapid discharge of the drug substance. They support moisture diffusion and dispersion of the tablet matrix. Tablet disintegration has received significant attention as an important step in obtaining fast drug release. The prominence on the availability of drug highlights the importance of the relatively swift disintegration of a tablet as a criterion for ensuring uninhibited drug dissolution performance[5].


© Copyright protected. Unauthorised republication, reproduction, distribution, dissemination and copying of this document in whole or in part is strictly prohibited.

**Types of Superdisintegrants**

*Natural Sources*: Pectin, Mucin, Agar, Alginic acid, Casein, Gelatin, Schizophillan, Carrageenin.

*Semi synthetic Sources*: Methyl cellulose (MC), Hydroxyl ethyl cellulose (HEC), Hydroxypropyl methyl cellulose (HPMC), Hydroxyethyl methyl cellulose (HEMC), Corboxymethyl cellulose (CMC).

*Synthetic Sources*: Povidone, Polyethylene glycol (PEG), polyvinyl pyrolidine (PVP), Crospovidone, Polyvinyl alcohol (PEA)

**Extended Drug Release Formulation**

Extended release drug delivery system attains a time-consuming release of the drug over acomprehensive period of time or the drug is engrossed over a longer period of time. Extended release dosage form at first releases a sufficient amount of drug to get the essential blood concentration (loading dose, DL) for the desired therapeutic reaction and therefore, further amount of drug is released at a controlled release rate (maintenance dose, DM) to maintain the blood levels for some desirable phase of time[6].

**Suitable Drug Candidate for Extended Release Drug Delivery System:**

It ought to be orally effective and firm in GIT medium. Drugs that have short half-life (2 – 4 hrs) make an excellent candidate for formulation into ER dosage forms.E.g. Captopril, Salbutamol sulphate. The dos e of the drug should be less than 0.5g as the oral path is appropriate for drugs given in dose as high as 1.0g.E.g. Metronidazole. Therapeutic range of the medicine must be high[7].

**Polymers used for extended release**

*Hydrogels*: Polyhydroxyethylmethylacrylate (PHEMA), Cross-linked polyvinyl alcohol (PVA), Cross-linked polyvinylpyrrolidone (PVP), Polyethylene oxide (PEO), Polyacrylamide (PA)

*Soluble Polymers*: Polyethylene glycol (PEG), polyvinyl alcohol (PVA), Polyvinylpyrrolidone (PVP), Hydroxypropylmethylcellulose (HPMC).

*Biodegradable Polymers*: Polylactic acid (PLA), Polyglycolic acid (PGA), Polycaprolactone (PLA), Polyanhydrides, Polyorthoesters.

*Non Biodegradable Polymers*: Polyethylene vinyl acetate (PVA), Polydimethylsiloxane (PDS), Polyether urethane (PEU), Polyvinyl chloride (PVC), Cellulose acetate (CA).

*Mucoadhesive Polymers*: Polycarbophil, Sodium Corboxymethyl cellulose, Polyacrilic acid, Tragacanth, Methyl cellulose, Pectin, Natural gums, Xanthan gum, Guar gum, Karaya gum

**Ajwain (*Trachyspermum Ammi*)**

Most of the kitchen elements are traditionally used as healing methods. Ajwian is used for cure of many diseases from earlier period.It is indigenous of Egypt and is cultivated in Iraq, Iran, Afghanistan, Pakistan, and India. In India, it is cultivated in Madhya Pradesh, Uttar Pradesh, Gujarat, Rajasthan, Maharashtra, Bihar and West Bengal. The fruits hold 2–4.4% brown colored oil known as ajwain oil. The main constituent of this oil is thymol, which is utilized as gastrointestinal ailments, devoid of appetite and bronchial illnesses[8].

**Pharmacological Profile of Ajwain**

Traditional therapeutic uses of Ajwain fruits include: galactogogue, stomachic, carminative, expectorant, antiseptic, amoebiasis andantimicrobial.Seeds deep fried in oil and used as a slenderbroth as a galactogogue, used in curing diarrhea, parasiticidal, and given in handling of amenhorroea, bronchitis, colic pain, antipyretic, febrifugal.It also treats abdominal tumors, abdominal pains, and piles. Occurrence of terpenes, glycosides and sterols in plant has been set up to exert active anti-inflammatory effects. It also possess Antihypertensive, antispasmodic and broncho-dilating activity, Hepatoprotective activity, Antilithiasis and diuretic activity, Abortifacient and galactogogic actions, Antiplatelet-aggregatory, Anti-inflammatory potential, Antitussive effects, Antifilarial activity, Gastro protective Activity, Detoxification of aflatoxins, Antimicrobial actions, Hypolipidaemic action, Anthelmintic Activity[9,10,11,12].

## MATERIALS AND METHOD

**Materials**

Ajwain (obtained from Dept. of Pharmacognosy, Nalla Narasimha Reddy School Pharmacy), ethanol, sucrose, mannitol, sodium starch glycolate, starch paste, eudragit, magnesium stearate and Hydroxy propyl methyl cellulose are acquired from SD fine chemical limited, Hyderabad.

**Equipment**

Weighing balance (SHIMADZU), Disintegration apparatus (LAB INDIA), Dissolution apparatus (LAB INDIA), UV-Visible spectrometer (ELICO SL210), Hot air oven (SISCO), pH apparatus (ELICO L1120), Heating mantle (SISCO), Bulk density apparatus (DBK), Capsule filling machine (SISCO) and Double cone blender (SISCO).

## METHOD

**Extraction Procedure**

A Soxhlet extraction is utilized when the preferred compound has a partial solubility in a solvent, and the impurity is insoluble in that respective solvent. It allows for unmonitored and unmanaged process while proficiently recycling a little amount of solvent to liquefy a larger amount of material. During each series, a part of the non-volatile compound dissolves in the solvent. After


© Copyright protected. Unauthorised republication, reproduction, distribution, dissemination and copying of this document in whole or in part is strictly prohibited.

many cycles the preferred compound is concentrated in the distillation flask.

**Formulation**

**Table 1:** Formulation

| Ingredients (Immediate Release) | Weight (gm) for 5gm granules | Justification |
|---|---|---|
| Ajwain extract (API) | 2.5g | Active pharmaceutical ingredient |
| Sodium starch glycolate | 2g | Super disintegrant |
| Magnesium stearate | 0.25g | Lubricant |
| Sucrose | 0.1g | Disintegrant |
| Mannitol | Qs | Bulk forming agent |
| Starch paste | Qs | Binding agent |
| **Ingredients (Immediate Release)** | **Weight (gm) for 5gm granules** | **Justification** |
| Ajwain extract | 2.5g | Active pharmaceutical ingredient |
| Eudragit | 2g | Sustained release Polymer |
| HPMC | 1.3g | Sustained release Polymer |
| Magnesium stearate | 0.25g | Lubricant |
| Sucrose | 0.1g | Disintegrant |
| Mannitol | Qs | Bulk forming agent |

**Method of Granule Preparation**

***Wet granulation***

Powder ingredients are weighed and mixed uniformly in double cone blender according to table 1.Weighed extract of Ajwain is added to the above blended powder - ajwain extract is semi liquid in nature and thus a binding agent is not added. Resultant mixture is uniformly mixed and then passed through sieve number 10.Larger granules are dried in hot air oven at 60°C for 60 minutes.The dried granules are further passed through sieve number 40 to prepare uniform sized granules. The granules are evaluated by the following parameters[13].

**Evaluation of Granules**

***Particle size analysis***

The size and size allocation of the granules produced was determined by agitation for 10 min with a sieve shaker fixed with a succession of standard sieves. From the weight retained on each sieve, a particle size distribution graph was plotted from which the mean diameter was calculated[14].

***Bulk density***

5g granules blend introduced into a dry 100 ml cylinder, without compaction. The granule was carefully leveled without compacting and the unsettled perceptible volume was read. The bulk density was calculated using the fallowing formula.

$$BulkDensity\ (\rho b) = \frac{Massofthe Powder\ (M)}{BulkVolume\ (Vb)}$$

***Tapped density***

Anappropriate amount of granules were placed in a 100ml measuring cylinder. After absorbing its first volume, the sample was tapped 500 times initially followed by an additional taps 750 times until the differentiation between succeeding dimension is less than 2% and then tapped volume, was measured, to the nearest graduated unit. Tapped density was calculated using equation[15].

$$TappedDensity(\rho t) = \frac{Massofthe Powder\ (M)}{TappedVolume\ (Vt)}$$

***Hausner's ratio***

$$Hausner's ratio = \frac{BulkDensity\ (\rho b)}{TappedDensity\ (\rho t)}$$

Lower hausner's ratio (<1.25) indicates better pour properties than higher ones, between 1.25 to 1.6 showing modest flow properties, cohesive powder and more than 1.5 poor flow.

***Carr's index***

A fixed amount of powder is dispensed into a measuring cylinder and its mass and volume are noted, tapped and bulk density are noted and Carr's index is found by using fallowing equation.

$$Carr's Index = \frac{\rho t - \rho b}{\rho t} \times 100$$

Carr's index values less than 18 are considered to be ranging from excellent to good and value from 23 are considered to possess very poor flow properties.

***Angle of repose***

**Fixed funnel method**

The substance is poured through a funnel to form a cone. The tip of the funnel should be held close to the growing cone and slowly raised as the pile grows, to minimize the impact of falling particles. Stop pouring the material when the pile reaches a predetermined height or the base a predetermined width.

$$Angleofrepose(\theta) = \tan -1\frac{h}{r}$$


© Copyright protected. Unauthorised republication, reproduction, distribution, dissemination and copying of this document in whole or in part is strictly prohibited.

$$\tan\theta = \frac{Heightof Pile\ (h)}{Radiusofpile\ (r)}$$

Where, h is the height of the powder cone and r is the radius of the powder cone. Values for angle of repose ≤ 30° usually show a free flowing material and angles ≥ 40° propose a poorly flowing material, 25-30 show good flow properties, 31-35 show good flow properties, 36-40 shows fair properties and 41-45 showing passable flow properties[15].

***Plotting of Calibration Curve***

Standard curve is a universal method for determining the concentration of a substance in an unknown sample by comparing the unknown to a set of standard samples of known concentration. Plotting of standard graph require determination of Lambda max. The graph is plotted using phosphate buffer of pH as a blank solution.

***Determination of λ max***

Take sample solution and in the cuvette and mix it well. Measure the absorbance or transmittance at different wavelengths. The minimum transmittance at a particular wavelength will correspond to maximum absorbance which will give $\lambda_{max}$.

**Standard graph**

The Ajwain extract was used prepared and dissolved in phosphate buffer which is also used as a blank solution. Eight standard dilutions were prepared by dilution of concentrated stock (1000mg/ml) using the concentration range of 0.2µg/ml-1.0µg/ml with the following formula and absorbance was determined by using UV-Vis Spectroscopy.

***Filling of Capsules***

Hard gelatin capsule shells are filled with extended release and immediate release granules according to table 2.

**Table 2: Filling of capsule shell**

| S. No. | Formulation | Immediate Release Granules | Extended Release Granules |
|---|---|---|---|
| 1 | F1 | 50mg | 250mg |
| 2 | F2 | 70mg | 230mg |
| 3 | F3 | 100mg | 200mg |
| 4 | F4 | 120mg | 180mg |
| 5 | F5 | 150mg | 150mg |
| 6 | F6 | 200mg | 100mg |
| 7 | F7 | 250mg | 50mg |

**Evaluation of Capsules**

***Weight variation***

Weigh individually 20 units selected at chance and calculate the average weight. Not more than two of the individual weights diverge from the average weight by more than the percentage given in the pharmacopoeia and not any deviates by more than twice that percentage[15].

***Drug content***

A dose of the immediate and extended release granules was accurately weighed and mixed in 100ml phosphate buffer Ph 6.8 in a volumetric flask. Succeeding dilution was made from the stock solution and the concentration of the dilution was measured at $\lambda_{max}$ at 219nm in spectrophotometer (UV). Drug content was found out from the fallowing equation[15].

$$DrugContent = \frac{Absorption \times Dilutionfactor}{Slope}$$

$$DilutionFactor = \frac{FinalVolume}{SoluteVolume}$$

***Disintegration***

Six capsules were positioned in each of the six tubes of the basket. Perforated plastic discs were then placed on the top of the capsules and the (pH 6.8) was used as dissolution media. Then the disintegration apparatus was run and test was carried out for all the formulations. According to I.P hard gelatin capsules should disintegrate within 30 minutes of administration[15].

***Dissolution***

The *in vitro* dissolution studies were carried out in USP dissolution test apparatus (dissolution tester USP) type 2 (basket model). A 700ml of dissolution medium (phosphate buffer pH 6.8) was taken in a covered vessel and the temperature was maintained at 37°C. The speed of the basket was set at 50rpm. Sampling was done at predetermined time intervals. For each sample 5ml of the dissolution medium was withdrawn and the same amount of dissolution medium was added to the dissolution medium. The sample withdrawn was filtered with whattman filter paper and diluted with phosphate buffer


© Copyright protected. Unauthorised republication, reproduction, distribution, dissemination and copying of this document in whole or in part is strictly prohibited.

to analyze in the UV spectrophotometer. The absorbance was noted; then cumulative % release was calculated.

## RESULTS AND DISCUSSION

### Preparation of Ajwain Extract

*Trachyspermum ammi* fruits are taken and the extract was prepared using ethanol as a solvent for extraction and soxhlet apparatus for the extraction procedure.

Process was done for 8 hours with multiple numbers of cycles, the obtained product has been heated at 50$^0$C to evaporate the solvent and concentrate the extract. A dark brown colored semi-solid product was collected and stored in fridge for further process.

### Formulation and Preparation of Granules

Ajwain extract was formulated for both immediate and extended drug release. For immediate drug release a superdisintegrant (Sodium Starch Glycolate) was added to the formulation. Eudragit and HPMC were formulated for extended release and the acquired granules are shown in figure no 1.

**Figure 1:** Ajwain extract granules

### Evaluation of Granules

#### *Particle size analysis*

The particle size analysis was done for both immediate and extended release granules and the results are shown in figure 2.

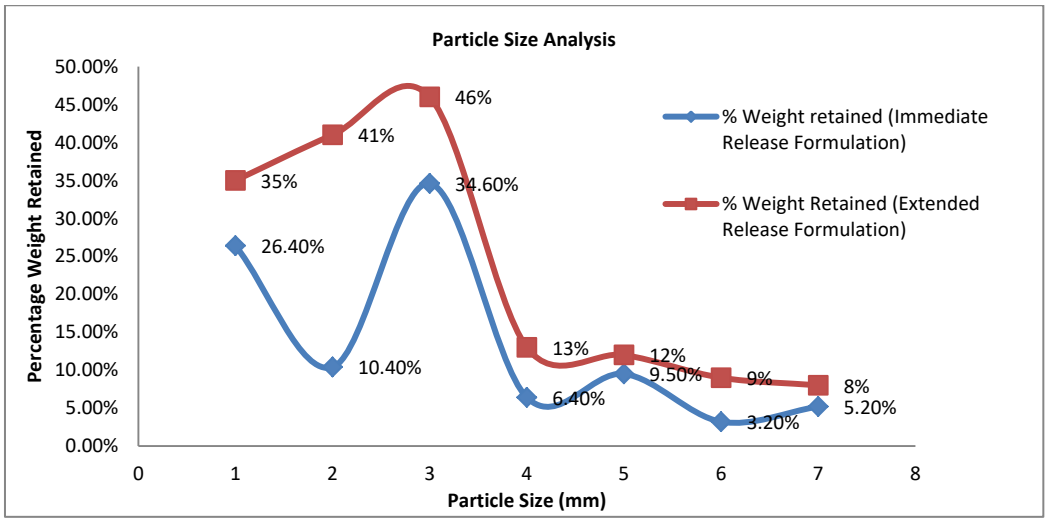


**Figure 2:** Particle size analysis of Immediate Release and Extended Release Formulation

Form the graphs it is clear that majority of the granules are retained on sieve no. 44 and the particle diameter range from 0.595 to 0.354mm in diameter. But in case of extended release formation the particles are greater in size; this behaviour is due to swelling of particles in presence of HPMC and eudragit.

#### *Flow properties of granules*

The values obtained for bulk density, tapped density, Hausner's ratio, Carr's index, and angle of repose are tabulated in Table 3. Both the formulations showed good flow properties as per the data provided. From the data of bulk and tapped density Hausner's ratio was found out to be 1.16 for I.R.G and 1.13 for E.R.G which showed GOOD flow properties as per standard values.

Carr's index of I.R.G and E.R.G are 14% and 12% respectively which enumerate EXCELLENT flow of granules.

Angle of repose study was conducted using fixed funnel method and the angles were 9.90 for I.R.G and 360 for E.R.G, which possess GOOD and EXCELLENT flow properties.

### Standard Graph in Phosphate Buffer of pH 6.8

#### *Determination of $\lambda_{max}$*

Maximum absorbance was determined in order to find out the maximum wavelength using UV-Spectrophotometer. The absorbencies were note at wavelength ranging from 200 to 400nm, and the maximum wavelength has been declared as 219nm for ajwain extract.

Standard Graph

From the lambda max data the calibration curve was plotted by taking 219nm as λmax, the concentration ranging from 2 µg/ml to 10 µg/ml were prepared by serial dilution method and absorbencies were determined using UV-Spectrophotometer and shown in figure 3. Regression value is 0.996 which magnifies the linear plot and slope was found out to be 0.074.


© Copyright protected. Unauthorised republication, reproduction, distribution, dissemination and copying of this document in whole or in part is strictly prohibited.

**Table 3:** Flow properties of I.R.G & E.R.G.

| Formulation | Bulk Density (g/ml) | Tapped Density (g/ml) | Hausner's Ratio | Carr's Index | Angle Of Repose | Flow Property |
|---|---|---|---|---|---|---|
| **Immediate release granules** | 0.37 | 0.42 | 1.16 | 14% | $9.9^0$ | GOOD |
| **Extended release granules** | 0.52 | 0.59 | 1.13 | 12% | $36^0$ | GOOD AND EXCELLANT |

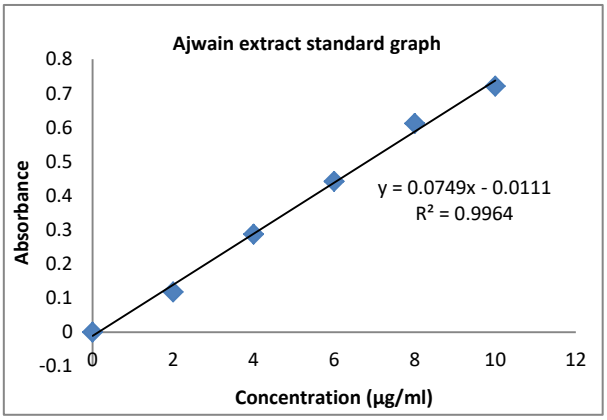


**Figure 3:** Ajwain extract standard graph

## Evaluation of Capsules

### *Weight Variation*

The capsules were filled with the combination of immediate release granules and extended release granules, according to requirement.

The average weight of 300mg granules within each capsule formulation was found to be uniform. This indicates uniform filling of granule blend during capsule filling. Not more than two of the individual weights deviated from the average weight by more than 10% and none deviated by more than twice that percentage, which provided good weight uniformity.

### Drug content

In all the 7 formulations, the values for drug content were found to be uniform and ranged between 98.3 and 102.7% of the theoretical value. The value ensures good quantity of the drug content in the capsules.

### Disintegration

All capsule shells started rupture in 3- 4 minutes and the complete rupture was at in 14-17minutes as range. Body and cap have ruptured at different timings started from 4 minutes to 9 minutes. The standard disintegration time limit for hard gelatin capsule shells was 30 minutes, thus the time of disintegration is within the limits.

### Dissolution

*In vitro* drug release was studied using IP 2 basket dissolution apparatus in 700 ml of pH 6.8 phosphate buffer at 37±0.5°C and at 50 rpm. An aliquot of 5 ml of the sample was withdrawn at regular intervals and the same volume of fresh dissolution medium was replaced. The samples withdrawn were filtered and drug content in each sample was analyzed after suitable dilution by UV-Spectrophotometer at 219 nm. The results are tabulated in table no 4.

The capsules were filled with immediate release and extended release granules with an aim to obtain instant relief and at the same point the release of drug will be prolonged to ensure continuous relief from illness. The dissolution studies state that for first 30 minutes drug release is rapid which is slowed down after the first half an hour, this is due to combination of both release pattern, and is publicized in figure 4.

F1 posses lower amount of I.R.G which have shown good amount of drug release during first 60 minutes that is 38.45%, while F 4 contain equal amounts of I.R.G % E.R.G and the release of drug was stagnant due to the formulation where 45.02% of drug was release and the rest of the dissolution study it has minimal release rate. F7 has a faster release rate when compared to all formulations as it has maximum quantity of I.R.G which has 82% of release in 60 minutes.

**Table 4:** Cumulative % drug release

| Formulation | Percentage of drug release | | | | | | |
|---|---|---|---|---|---|---|---|
| | 5min | 15min | 30min | 60min | 90min | 120min | 180min |
| F1 | 12.05 | 15.36 | 35.68 | 38.45 | 41.08 | 43.28 | 45.27 |
| F2 | 17.32 | 21.57 | 28.79 | 31.45 | 34.22 | 38.43 | 44.69 |
| F3 | 22.56 | 24.21 | 35.2 | 41.08 | 43.58 | 45.71 | 49.21 |
| F4 | 28.74 | 31.56 | 38.64 | 45.20 | 56.03 | 62.87 | 68.47 |
| F5 | 32.63 | 46.31 | 58.47 | 65.51 | 71.46 | 74.8 | 75.2 |
| F6 | 38.57 | 48.89 | 62.03 | 75.02 | 74.21 | 78.56 | 81.27 |
| F7 | 45.21 | 65.28 | 79.64 | 82.14 | 83.24 | 86.75 | 92.12 |


© Copyright protected. Unauthorised republication, reproduction, distribution, dissemination and copying of this document in whole or in part is strictly prohibited.

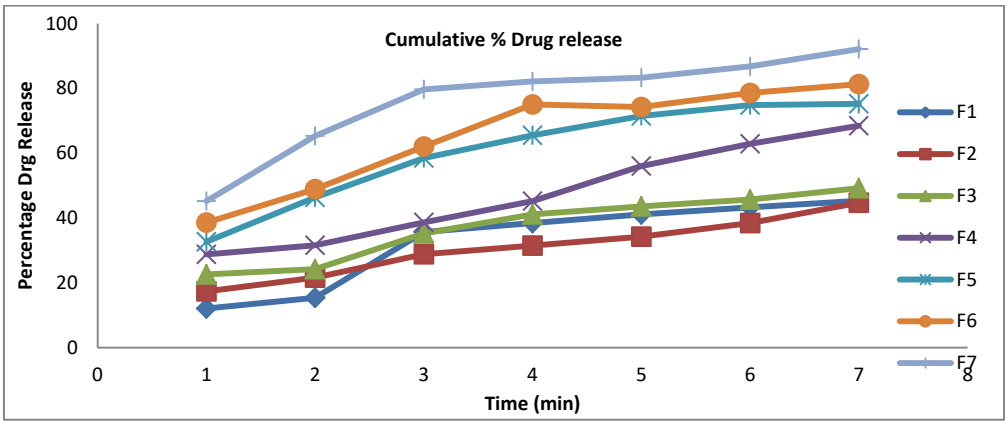


**Figure 4:** Cumulative % drug release

This makes clear that F1 is suitable for lower intensity of disease where prolonged release plays a key role; F7 is adequate, where the patient would get instant relief and at the same point as extended release would be beneficial.

## CONCLUSION

Ajwain fruits were used for extraction purpose which resulted in formation of dark colored semi-solid product. The extract have been formulated as granules along with supdisintegrants (sodium starch glycolate) or extended release polymers (HPMC, Eudragit) and the other Excipients such as glidants, lubricant, and filler are added. The resultant granules were evaluated for flow properties and particle size, and the results elucidated GOOD flow properties of both immediate and extended release granules. The ajwain extract filled capsules were evaluated for weight variation, drug content, and disintegration time and dissolution studies. From the results it is evident that all the formulations were within the range of I.P limits. *In-vitro* dissolution study enumerated that the formulation F1 showed slower release rate than compared to other formulations. Formulation F7 has rapid rate of drug release due to high proportion of immediate release formulations.

From this work it can be concluded that Ajwain 9 *Trachyspermum ammi*) which is traditionally used to treat various disease condition and it can be administered in rapid release and prolonged release dosage forms.

## REFERENCES

1. Chung,K.F., current and future properties for drugs to suppress cough, IDrugs, 6, 2003, 781-786. DOI:10.1371; PMID: PMC4018403.
2. Prabhakar C, BalaKrishna K., A review on effervescent tablets, Int J Pharm Tech, 3, 2011, 704-712.
3. Patel JB, Suhagia BN, Patel MN, Patel BT, Patel AM, Patel TR, Preparation and evaluation of effervescent tablets of ibuprofen, WJPPS, 2(4), 2013, 2145-2155. DOI: 10.20959; PMID: 20177-9433.
4. Tripathi KD. Essentials of medical pharmacology. Edn 6, Jaypee Brothers Medical Publishers Ltd, New Delhi, 2007, 155-157.
5. Lachmann L, Lieberman H, Kanig J. The Theory and Practice of Industrial Pharmacy. Edn 3, Varghese Publishing House, Bombay, 1991, 320-321.
6. Loyd VA, Nicholas CP, Howard CA. Ansel's Pharmaceutical dosage form and drug delivery system. Edn 9, Lippincott Williams and Wilkins, Philadelphia, 2011, 198-200.
7. Howard C Ansel, Nicholas G Popvich, Loyd V Allen. Pharmaceutical Dosage Forms and Drug Delivery System, First Edition, 1998, pp 78.
8. Holliday SM, Benfield P. Venlafaxine, A review of its pharmacology and therapeutic potential in depression drugs, Drugs, 49, 1995, 280–94. PMID: 7729333.
9. Chauhan B, KumarG,Ali M., Review on phytochemical constituents and activities of *Trachyspermum ammi* (L) sprague fruits, AJPTR, 2(4), 2012, 329-340. DOI: 10.2337; PMID: 19118286.
10. Ishikawa T, Sega Y, Kitajima J., Water-Soluble Constituents of Ajowan, ChemPharmaceut Bull., 49(7), 2001, 840-844. DOI: 10.1248; PMID: 28674344.
11. Gang SK, Sharma ND, Gupta SR., A Phenolic glucoside from the seeds of *carumcopticum*, Phytochemistry, 9(10), 1980, 2215-2216. DOI: 10.1016; PMID: 28658609.
12. Qureshi AA, Kumar KE. Phytochemical constituents and Pharmacological activities of *Trachyspermum ammi*. Plant Archives, 10(2), 2010, 955-959.
13. Rajalakshmi G, Vamsi CH, Balachander R, Damodharan N., Formulation and evaluation of diclofenac potassium effervescent tablets, Int J Pharm Biomed Res, 2(4), 2011, 237- 243.DOI: 10.7439.
14. Nagendrakumar D, Raju SA, Shirsand SB, Para MS, Rampure MV, Fast Dissolving Tablets of Fexofenadine HCl by Effervescent Method, Indian J Pharm Sci, 71(2), 2009, 116-9. DOI: 10.4103; PMID: 20336204.
15. Srinath KR, Chowdary P, Palaniswamy P, VamsyKrishna A, Aparna S, Ali SS, Formulation and evaluation of effervescent tablets of Paracetamol, IJPRD, 3(3), 2011, 76-104.DOI:n/d.

**Source of Support:** Nil, **Conflict of Interest:** None.


© Copyright protected. Unauthorised republication, reproduction, distribution, dissemination and copying of this document in whole or in part is strictly prohibited.