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FORMULATION AND EVALUATION OF IBUPROFEN EFFERVESCENT TABLETS

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ABSTRACT

The formulation and evaluation of ibuprofen effervescent tablets have gained significant attention due to their potential advantages over conventional tablet formulations. This study aimed to develop an effective and stable formulation of ibuprofen effervescent tablets with improved drug dissolution and patient compliance. Various formulations of ibuprofen effervescent tablets were prepared using different excipients and evaluated for their physicochemical properties and in vitro drug release profile. The tablets were formulated using a direct compression method, incorporating ibuprofen as the active pharmaceutical ingredient along with effervescent agents, binders, disintegrants, and lubricants. the formulation and evaluation of ibuprofen effervescent tablets proved successful in developing a stable and effective formulation with improved drug release properties. These effervescent tablets have the potential to provide faster and more efficient pain relief, making them a promising alternative to conventional ibuprofen tablets. Further studies, including in vivo evaluations and clinical trials, are warranted to validate their therapeutic efficacy and safety. Because they are simple to use and improve compliance, fast-dissolving drug delivery systems have recently begun to acquire popularity and acceptance as innovative drug delivery systems. Elderly folks often have trouble taking the tablet. Ibuprofen prevents peripheral tissue from producing prostaglandins (PG). The purpose of this research was to create effervescent tablets with enough mechanical integrity and to have them dissolve more quickly in water. A compatibility examination of the drug's acids, bases, and other excipients was carried out in the pre-formulation research, indicating that they are compatible with one another. Various acids

and bases were based in combination to make tablets. Additionally, tablets made with various binding agents were tested for effervescences, hardness, friability, solution time, and pH. Tablets made with a greater ratio of citric acid to sodium bicarbonate with pvp-K30 2% as the binder exhibit a quick solution time, a higher pH, and excellent hardness.

Keywords: Ibuprofen, Effervescent tablets, Physicochemical properties, Drug dissolution, Patient compliance, Excipients, Effervescent agents, Binders, Drug content uniformity

INTRODUCTION

However, there are important disadvantages, such as slow absorption and a prolonged beginning of effect, oral dosage forms remain the most common method of medicine administration. The medicine may be administered in liquid form to get around this, however many APIs only have a limited amount of stability in liquid form. Effervescent tablets serve as a substitute dose form as a result. Just before to administration, the tablet is dissolved into a glass of water, and the medication solution or dispersion is then instantly consumed. Due to the interaction between tartaric acid and citric acid with alkali metal carbonates or bicarbonates in the presence of water, the tablet soon breaks apart by internal CO2 release in water **[1]**. Saline cathartics were accessible as effervescent powders in the seventeenth century, and these powders were later included as compound effervescent powders in official compendia. 'Seidlitz powders' was the popular name for them. Since they provided the public with a distinctive dosage form that was entertaining to create in addition to the medical benefit of the specific treatments, effervescent mixes have gained some degree of popularity throughout time. Additionally, they had a tasty flavour because to carbonation, which served to cover up the unpleasant taste of the medications **[2]**. The formulation of effervescent granules relies on the demands of the production process as well as the need to create a preparation that dissolves in water. A minimum of one acid and a minimum of one base must be present. When the base and acid react, carbon dioxide must be released. Examples of these acids and bases include sodium carbonate, potassium bicarbonate, and sodium bicarbonate. Examples of such acids include tartaric acid and citric acid. Because using either acid alone presents challenges, effervescent granules are often made from a mix of citric and tartaric acids rather than from a single acid. When tartaric acid is the only acid present, the resultant granules are mechanically weak and easily crumble. When used alone, citric acid produces a sticky slurry that is difficult to granulate throughout production **[3]**. The fact that the medication substance is already in solution when the tablet is ingested is a key benefit

of effervescent tablets. As a result, the absorption is quicker and more thorough than with traditional tablets. A speedier start of effect results from a faster absorption. Effervescent medications are administered to the stomach at a pH level ideal for absorption. Many medications take a long time to pass through the GIT or have poor absorption when taken with food or other medications. Tablets that are effervescent completely dissolve in a buffered solution. Less localised touch means less discomfort and more tolerance in the upper GIT. Buffering also prevents stomach from being caused by gastric acids, which may interfere with the medicine itself **[4, 5]**. It is difficult to provide a dosage form that contains NSAIDs along with excipients necessary for the formulation of the tablet into the dosage form and excipients necessary to ensure rapid disintegration, while also avoiding the provision of tablets that are either too large for patient consumption or cannot be produced using a standard large-scale manufacturing process **[6]**. Several clinical research have also shown a correlation between the plasma ibuprofen levels and the onset and potency of the analgesic effects. The amount of ibuprofen has a stronger analgesic effect. According to a different research, soluble Ibuprofen begins to reduce pain before Ibuprofen pills do. The organic acid ibuprofen has a low solubility. The solubility of the acid increases dramatically only at a pH-value of 7, when it forms a salt (pK-value of ibuprofen acid is 4.5). Given how widely Ibuprofen is used, it would be very beneficial if Ibuprofen acid could be made to dissolve more quickly and less pH-dependently without affecting the manufacturing of the medication **[7-11]**. Tablets are a pharmaceutical solid unit dose form of medication or medications, manufactured either by compression or moulding and with or without acceptable excipients. It consists of a combination of active ingredients and excipients that are often ground, compressed, or pressed into solid doses. Poorly soluble medication fast dissolving tablets will provide prompt and efficient therapeutic action. The current research is focused on quick disintegration of tablets, which is the first stage for fast dissolving tablets of poorly soluble medicine, mainly IBUPROFEN, in order to produce this type of tablets originally. The most common method of taking medicine is by oral dosage forms, despite important disadvantages such slow absorption that prolongs the time before effect occurs. This can be overcome by administration of the drug in liquid form but many API's having limited level of stability in liquid form. So selected IBUPROFEN is formulated into the Effervescent Tablets which acts as an alternative dosage form.

Hence the aim of the present study is to increases the absorption as well as to

show the quick onset of action by formulating the ibuprofen effervescent tablets.

MATERIALS AND METHODS

Ibuprofen (Gift sample from vasudha pharmaceutical, vizag, india), Citric acid (Qaligens fine chemicals, Mumbai), Tartaric acid (Qualigens fine chemicals, Mumbai), Sodium carbonate (SD fine chem. Limited.), Microcrystalline cellulose (MCC) (Central drug house private limited), Sodium Starch Glycolate (SSG) (Lobachemie private limited), Magnesium stearate (Lobachemie private limited), Talc (Lobachemie private limited)

METHODS

PRE-FORMULATION STUDIES: [12-18]

The initial stage in the logical creation of a pharmacological substance's dosage form is pre-formulation research. A pre-formulation study's goal is to gather knowledge about the drug ingredient in order to help with formulation development. Pre-formulation is the process of researching the physical and chemical characteristics of the drug material both on its own and when mixed with an excipient.

Pre-formulation research aim to pinpoint the physicochemical characteristics and excipients that could have an impact on the formulation, manufacturing process, and pharmacokinetic and biopharmaceutical characteristics of the final product. The pre-formulation research involves the following tests:

1. Organoleptic characteristics.
2. Solubility study.
3. Melting point.
4. Standardization of the drug (calibration curve).
5. Compatibility study (FTIR spectrophotometry).

1. Organoleptic Characteristics: The color, odor and taste of the drug were characterized and recorded using descriptive terminology.

2. Solubility Study: The solubility of ibuprofen was determined as per BCS. The solubility was checked in 250ml of 0.1N HCL and buffers with in pH range 2-8 and in water.

3. Melting Point: Temperature at which the solid and liquid forms of a pure substance can exist in equilibrium. As heat is applied to a solid, its temperature will increase until the melting point is reached.

4. Standardization of the Drug (calibration) curve):

4.1. Preparation of 0.1 N Hydrochloric Acid (pH 1.2):

8.5 ml of concentrate hydrochloric acid was taken and diluted with distilled water up to 1000 ml.

4.2. Determination of λmax of Ibuprofen in 0.1N HCl:

When 50 ml of 0.1N HCl and 50 mg of ibuprofen are combined, they provide a

concentrated stock solution with a concentration of 1000 g/ml. When 1 ml of the working standard solution is diluted to 100 ml with 0.1 NHCl, the resultant concentrated solution has a concentration of 10 g/ml. This solution was scanned using light with a wavelength between 200 and 400 nm, and the accompanying scan spectrum curve was observed. The highest absorption wavelength for that wavelength is noted as λmax.

4.3. Construction of calibration curve of Ibuprofen in 0.1N HCl:

Ibuprofen was weighed, dissolved in 50ml of 0.1N HCl, and then diluted to a volume of 50ml using 0.1N HCl to produce a concentrated stock solution with a concentration of g/ml. 1 ml of the working standard solution was diluted to 100 ml with 0.1 N HCl, yielding a concentrated solution with a concentration of 10 g/ml. To create concentrated solutions containing 10, 20, 30, 40, or 50 g/ml, take 1, 2, 3, and 5 ml of the solution from dilution 1 and dilute it up to the specified level in a 10 ml volumetric flask. The maximum absorbance of this solution was recorded at λmax 248 on the calibration curve of ibuprofen in 0.1N HCL.

Observation: At 248 nm Calibration curve was plotted using the concentrations 0, 10, 20, 30, 40, 50µg/ml and was found regressive value 0.999 and hence it is indicating drug following beer's lamberts law.

Formulation of Tablets:

Table 1: Concentrated Solutions and Their Absorbance

Concentration (µg/ml)	Absorbance
0	0
10	0.175
20	0.132
30	0.196
40	0.261
50	0.325

Table 2: Composition of Tablets by using Direct Compression:

Formulation (1): Composition of Tablets by using SSG

S.NO	API	Citricacid	Tartaric acid	Sodium bicarbonate	MCC	SSG	Magnesiumstate	Talc
1.	200mg	35mg	50mg	45mg	135mg	30mg	2.5mg	2.5mg
2.	200mg	35mg	50mg	45mg	115mg	60mg	2.5mg	2.5mg
3.	200mg	35mg	50mg	45mg	75mg	90mg	2.5mg	2.5mg
4.	200mg	35mg	50mg	45mg	65mg	100mg	2.5mg	2.5mg
TOTAL WEIGHT=500MG								

Formulation (2): Composition of Tablets by using CSS

S.NO	API	Citricacid	Tartaric acid	Sodium bicarbonate	MCC	CSS	Magnesiumstate	Talc
1.	200mg	35mg	50mg	45mg	135mg	30mg	2.5mg	2.5mg
2.	200mg	35mg	50mg	45mg	115mg	60mg	2.5mg	2.5mg
3.	200mg	35mg	50mg	45mg	75mg	90mg	2.5mg	2.5mg
4.	200mg	35mg	50mg	45mg	65mg	100mg	2.5mg	2.5mg
TOTALWEIGHT=500MG								

Method of preparation of the tablet by direct compression method:

- Ibuprofen, citric acid, tartaric acid, sodium carbonate and other excipients are accurately weighed according to the formula and transferred into mortar.
- The compounds were then grinded into fine particles.
- The fined powder was transferred through sieve no 80# for identification of larger particles.

Finally, the powder is further carried out for compression using tablet compression machine

EVALUATION OF EFFERVESCENT TABLETS

1. PRE-COMPRESSION STUDIES

1.1 Bulk Density:

It refers to packing of particles. Bulk density is used to determine the amount of drug that occupies the volume in gm/ml.

Procedure:

Ibuprofen was weighed and then transferred without tapping into a 100ml measuring cylinder. It was measured how much space the medication took up. In order to quantify bulk density, a formula was used.

Pi =m\Vi

Where, m=mass of the blend.

Vi=untapped volume.

1.2 Tapped Density:

The volume of the medicine in a graduated cylinder after it had been weighed was recorded. After that, a tapped density instrument applied 100,500,750 taps to the cylinder. According to USP, the mixture underwent 500 taps. Calculated volume variation was sent through an additional 750 taps. Calculated percentage variation,

Pt = m\Vt

Where, Vt=tapped volume.

1.3 Carr's Index [Compressibility]:

The property of the powder to be compressed is measured by the compressibility index and the hausner's ratio. The drug's packing capacity was assessed based on the volume change that resulted from packing rearrangement during tapping. Carr's compressibility index is what it is called, and its calculation is as follows:

Carr's index = [tapped density-bulk density\bulk density] X 100

1.4 Hausner's Ratio: It is measurement of fractional resistance of the drug. The ideal range should be 1.2-1.5. It was determined by the ratio of tapped and bulk density.

Hausner's ratio = tapped density-bulk density

1.5 Angle of Repose:

It is defined as maximum angle that can be obtained between the free scanning granule heap and horizontal plane, which is given by the equation

$\Theta = \tan^{-1} h\backslash r$

Where, Θ=angle of repose, h=height of granule heap, r= radius

of granule cone

Procedure:

A measured amount of the medication was poured via a funnel that was 2 cm above the ground. The powder is carried via a heat-forming zone until it reaches the funnel's tip. Utilizing the mentioned formula, the radius was measured and the angle of repose was calculated.

Table 3: Interpretation of Granules Flow:

FLOW CHARACTER	COMPRESSIBILITY INDEX [%]	HAUSNER'S RATIO	ANGLE OF REPOSE
Excellent	0-10	1.00-1.11	25-30
Good	10-15	1.12-1.18	31-35
Fair	16-20	1.19-1.25	36-40
Passable	21-25	1.26-1.34	41-45
Poor	26-31	1.35-1.45	46-55
Verypoor	32-37	1.46-1.59	56-65
Extremelypoor	>38	>1.60	>66

2. POST COMPRESSION STUDIES

Prepared effervescent tablets were evaluated for following parameters

2.1. Physical characterization

2.2 Physical appearance

2.2.1 Hardness,

2.2.2 Thickness

2.2.3 Weight variation

2.2.4 Friability

2.2.5 Effervescent time

2.2.6 Content uniformity

2.2.7 Moisture content

2.2.8 Disintegration time

2.2.1 Hardness: A tablet has a certain degree of mechanical strength in it that allows it to endure handling during manufacturing, shipping, and dispensing. The Monsanto hardness tester is the instrument that is most often used to assess the crushing strength of tablets.

Method: A schleuniger hardness tester was used to assess the hardness of ten tablets that were chosen at random. The median was used to measure tablet hardness.

2.2.2 Thickness: Ten tablets were selected at random from each formulation, and the thickness of each tablet was measured accurately using a vernier caliper scale.

2.2.3 Weight variation:

Twenty tablets were selected at random, and the average weight was calculated. The weight of each pill was compared to the weight of all tablets combined.

Table 4: Limits of Weight Variations

Avg. weight (mg)	Maximum % difference allowed
<130	±10
130-324	±7.5
>324	±5

2.2.4 Friability: It has to do with the tablet's capacity to survive shocks and abrasion without breaking while being manufactured, packed, transported, and handled by customers. The Roche friabilator is a friability test device that may be used to assess friability. In general, compressed tablets that lose between 0.5% and 1.0% less weight is regarded as acceptable.

Method: Ten tablets were first weighed before being transferred to the Rocha friabilator. In 4 minutes, it underwent 100 rotations. The pills were cleaned and given a new final weight. The following formula was used to apply these two weights, and friability was computed.

$$\% \text{ Friability} = \frac{\text{(Initial weight - final weight)}}{\text{(Initial weight)}} \times 100$$

2.2.5 Effervescent time:

A beaker holding 200 ml of filtered water and one tablet was used. Effervescence time ends when a clean solution free of particles is attained.

2.2.6 Content uniformity:

For the purpose of measuring the quantity of the active component, 10 tablets from each formulation were randomly chosen. No pill should fall outside of the formula's specified range (90–110%) or have a coefficient of variation greater than 6. 20 tablets must be checked even if just one tablet was beyond the 80-120% range and preceding range. Any one of these 20 tablets should not go beyond the range of 90-110 percent.

2.2.7 Moisture Content:

Ten tablets of each formulation were dried for four hours in a desiccator with activated silica gel. 0.5% or less water content is acceptable.

2.2.8 In - Vitro Disintegration Test:

The USP disintegration test instrument was used to determine the disintegration time. Six pills were chosen at random from each batch to undergo a disintegration test. At a temperature of 37 °C, the test was conducted in 900 ml of buffer solution that is appropriate for certain tablets.

Standard plot of ibuprofen

It was plotted by taking absorbance on X – axis and concentration (µg/ml) (X) on Y – axis, the plotted is shown below

RESULTS AND DISCUSSIONS

PREFORMULATION STUDIES: [19-22]

Solubility Profile:

The solubility study was conducted in various solvents and found soluble in methanol, ethanol and found insoluble in water.

Melting point:

The melting point of ibuprofen was found to be 158^0 C **(Table 5)**.

(Figure 1).

A good and practical analytical approach should be needed for the measurement of ibuprofen in the tablets and to verify if the

medication is adhering to Beer Lambert's law. This is accomplished by utilizing a Lab India (UV-3000) double beam spectrophotometer and 0.1N HCl (pH 1.2) as the dilution medium. The maximum wavelength (max) was discovered to be 248 nm, which was in good agreement with the values given in the literature. The absorbance at this wavelength was measured using the standard dilutions (10–50 g/ml) in triplicate, and the findings indicated satisfactory linearity (R2=0.991).

POST COMPRESSION STUDIES: (Table 6)

All post-compression investigations, including weight change and friability, were examined for the prepared formulations 1 and 2 from direct compression procedures. The preceding table, which includes all of the test results that were seen to be within acceptable limits, shows that:13 Direct compression techniques revealed that the hardness of formulations 1 and 2 was in the range of 2.32 and 2.70, respectively. which are suitable for handling and storing tablets made from specified formulations. The findings for effervescent time and disintegration time were found in the ranges of 120 - 545 sec (2- 9.08 min), 52 - 320 sec (0.52 - 5.33 min), respectively. The effervescent duration is significant according to the current experiment **(Table 7, Figure 2)**.

The primary determinant of tablet disintegration is the effervescent time from the tablets, and the direct compression technique revealed that the effervescent times of manufactured formulations 1 and 2 were 120–545 sec and 302–691 sec, respectively **(Table 8)**.

Disintegration time for all the formulations were carried. Observed Disintegration times for the tablets prepared by direct compression method was from 146- 450sec **(Figure 3, 4)**.

The purpose of the present study is to develop fast-dissolving tablets employing direct compression and effervescent mixes of SSG and CSS. **Table 8** displays the findings of the disintegration research for all formulations. When utilizing CSS, F8 from FORMULATION 2 dissolved with the shortest disintegration time, or 146 seconds. In this investigation, we found that the disintegration of the tablets was quicker for those made via direct compression using CSS than for those made using SSG.

Table. 5: Calibration of ibuprofen

Concentration (µg / ml)	Absorbance at 248 nm
0	0
10	0.075
20	0.132
30	0.196
40	0.261
50	0.325

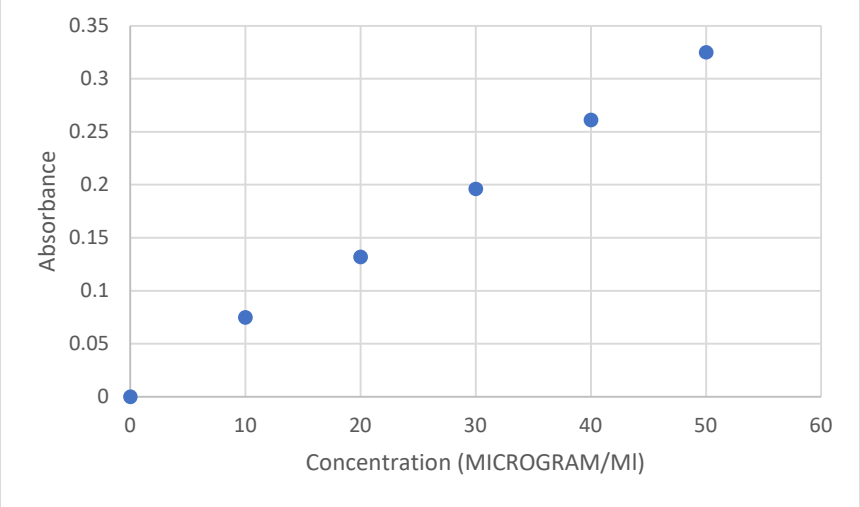

Figure 1: Standard Calibration Curve for ibuprofen

Table 6: Results of post compression studies

DIRECT COMPRESSION METHOD FORMULATION (1)						
Formulations	**Weight variation**	**Friability**	**Hardness**	**Drug content (%)**	**Effervescenttime**	**Dis-integration time**
F-1	**±1.9**	**0.34**	**2.50**	**99.74±0.40**	**691**	**450**
F-2	**±2.9**	**0.40**	**2.40**	**99.60±0.70**	**654**	**413**
F-3	**±3.8**	**0.37**	**2.60**	**99.65±0.90**	**615**	**405**
F-4	**±3.8**	**0.41**	**2.32**	**99.86±0.25**	**510**	**301**

DIRECT COMPRESSION METHOD FORMULATION (2)						
Formulations	**Weight variation**	**Friability**	**Hardness**	**Drug content (%)**	**Effervescenttime**	**Disintegrationtime**
F-5	**±4.2**	**0.45**	**2.65**	**99.69±0.70**	**475**	**275**
F-6	**±2.5**	**0.48**	**2.55**	**99.73±0.30**	**421**	**218**
F-7	**±4.0**	**0.30**	**2.40**	**99.74±0.25**	**375**	**177**
F-8	**±2.3**	**0.51**	**2.30**	**99.78±0.40**	**335**	**146**

Table 7: Effervescence time of tablets:

Formulations	**Direct CompressionMethod**
	Effervescent time (Sec)
F-1	**691**
F-2	**654**
F-3	**615**
F-4	**510**
F-5	**475**
F-6	**421**
F-7	**375**
F-8	**335**

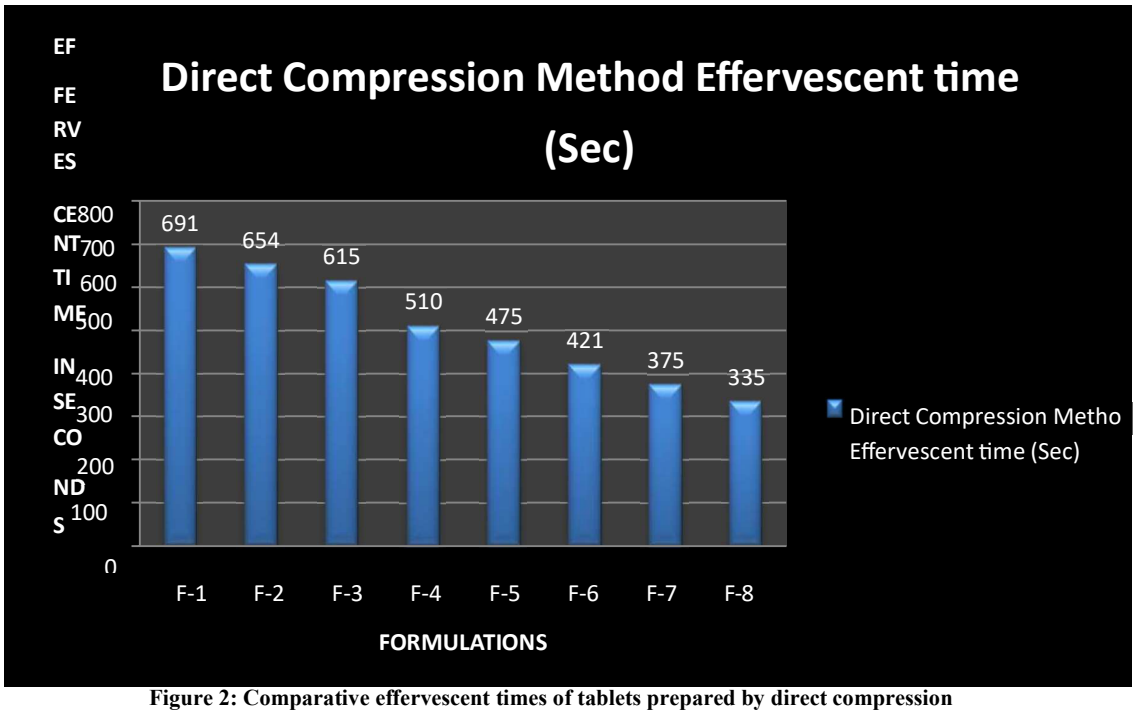

Figure 2: Comparative effervescent times of tablets prepared by direct compression

Table 8: Disintegration time of tablets:

Formulations	Direct Compression Method
	Disintegration time(Sec)
F-1	450
F-2	413
F-3	405
F-4	301
F-5	275
F-6	218
F-7	177
F-8	146

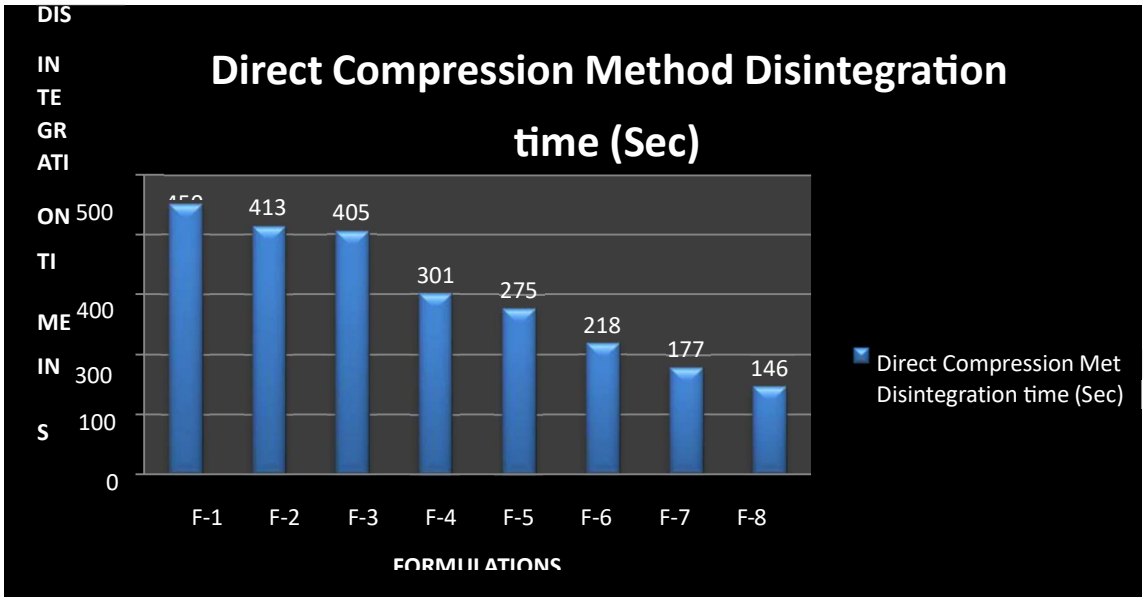

Figure 3: Comparative Disintegration times of tablets prepared by Direct compression

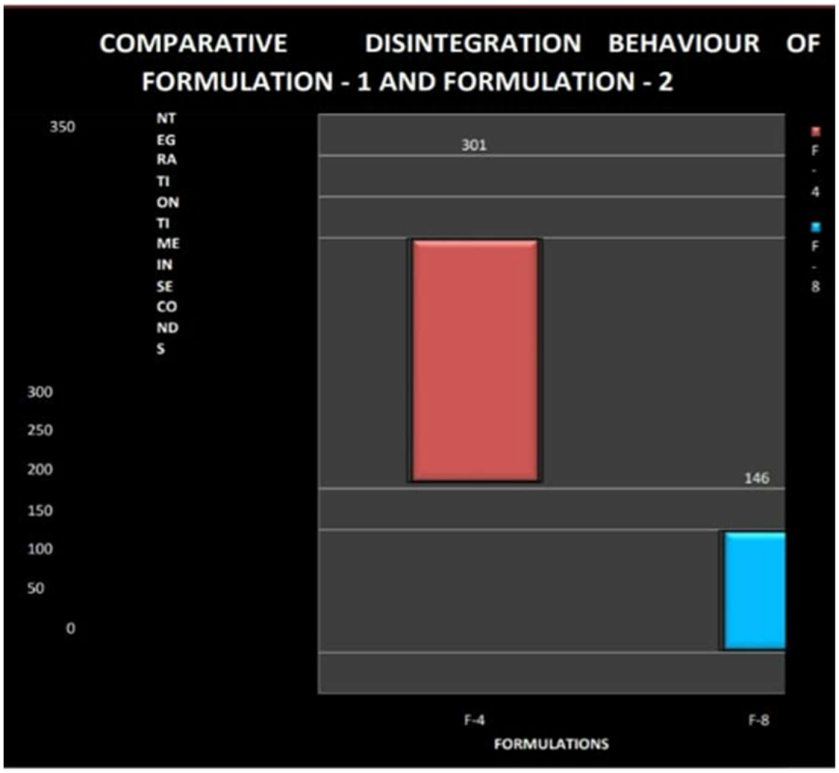

Figure 4: Comparative Disintegration times study of tablets prepared by direct compression by using SSG and CSS

CONCLUSION

The fast dissolution tablets of ibuprofen might be better, practical approach to achieve a better therapeutic action. This can be achieved by considering both fast disintegration of tablet and solubility enhancement of the drug. In this present study, fast disintegrating tablets were prepared successfully using effervescent mixture at different possible concentrations by direct compression method by using SSG and CSS. The following studies like melting point, solubility, and UV analysis of were complied with literature values. The post compression studies like hardness, friability, weight variation, drug content etc., were analyzed and found acceptable as per the official limits. This study indicated that the lesser effervescent time of the tablets will have fast disintegration. From the comparative study of the formulations for disintegration behavior, the fast-disintegrating formulation among all from FORMULATION (1): F4 IS disintegrated within 301 seconds and the fast-disintegrating formulation among all from FORMULATION (2): F8 disintegrated within 146 seconds. Hence, the study revealed that fast disintegrating tablets can be prepared using effervescent mixtures by using CSS at different concentrations at optimum conditions. As the super disintegrating agents are the common source for the development of fast disintegrating

tablets, the present study initiated using effervescent mixture for the disintegration effect of the tablets and showed disintegration within a minute.

REFERENCES

[1] Srinath KR, Chowdary P, Palanisamy P, Vamsy K, Aparna S and Ali S, "Formulation and evaluation of effervescent tablets of Paracetamol. Int. J. Pharm. Res. Dev. 2011: 2(12):76- 104.

[2] Ali K, Effervescent granules and methods for their preparation, http://www.pharmainfo.net/reviews/review-patents-effervescent-granules.

[3] Parikh D, Handbook of Pharmaceutical Granulation, Marcel Dekker Inc New York, 1997: pp 339.

[4] Stahl H, "Drying of pharmaceutical granules in single pot systems." Pharm. Ind. 1999; 7(61):656-661.

[5] Roscheisena G and Schmidt P, "Preparation and optimisation of leucine as lubricant for effervescent tablet formulations." Pharma.Acta.Helv. 1995; 2(70):133-139.

[6] Rotthauser B, Kraus G and Schmidt P, "Optimization of an effervescent tablet formulation containing spray dried L-leucine and polyethylene glycol 6000 as lubricants using a central composite design." Eur.J.Pharm.Biopharm. 1998; 6(46):85-94.

[7] Arnett F, "The American Rheumatism Association 1987 Revised Criteria for the Classification of Rheumatoid Arthritis." Arthritis Rheum 1988; 31: 315.

[8] Anna Livshits, Ronit Machtinger, Liat Ben David, Maya Spira, Aliza Moshe-Zahav, Daniel S. Seidman , Ibuprofen and paracetamol for pain relief During medical abortion : a double-bliend randomized controlled study, Fertility and Sterility, 2009; 91(5) : 1877- 1880.

[9] Babiloni C, Frisoni GB, Del Percio C, Zanetti O, Bonomini C, Cassetta E, Pasqualetti P, Miniussi C, De Rosas M, Valenzano A, Cibelli G, Eusebi F, Rossini PM., Ibuprofen treatment modifies cortical sources of EEGrhythms in mild Alzheimer's disease, 2009; 120(4):709-718.

[10] Mannila A, Rautio J, Lehtonen M, Järvinen T, Savolainen J ,Inefficient central nervous system delivery limits the use of ibuprofen in neurodegenerative diseases. Eur J Pharm Sci. 2005 ; 24(1):101-5.

[11] Abolfazl Aslani, Fatemeh Fattahi, Formulation, Characterization and Physicochemical Evaluation of Potassium Citrate Effervescent Tablets, Advanced Pharmaceutical Bulletin, 2013; 3(1), 217-225.

[12] P.V. Swamy *et al* developed pheniramine maleate orodispersible tablet with patient compliance by effervescent methods. Researcher used

the sodium bicarbonate and tartaric acid along with different super disintegrating agents like pregelatinized starch, sodium starch glycolate, croscarmellose sodium and crospovidone. (Swamy *et al*. 151-54).

[13] Setty C.M. *et al.,* tried to formulate potassium citrate effervescent tablets by direct compression, fusion and wet granulation techniques. (Setty *et al* . 180).

[14] Y.W. Chien, Novel drug delivery systems. In: Drug and Pharmaceutical Sciences, 2nd ed., Marcel Dekker Inc. New York, 1992:1-139.

[15] D.M. Brahmankar, S.B. Jaiswal, Biopharmaceutics and pharmacokinetics, A Treatise, 2nd ed., Vallabh prakashan, New Delhi, 2009:345-47.

[16] S.Chandran, Controlled release preparations have been reported to reduce the gastro irritant and ulcerogenic effects of non-steroidal anti-inflammatory drugs, Indian J. Pharm. Sci., 2008, 70 (2): 596-602.

[17] G.S. Sonar, A bilayer and floating-bioadhesive drug delivery system exhibiting a unique combination of floatation and bioadhesion to prolong residence in the stomach using Ibuprofen as a model drug, Indian J. Pharm. Educ. Res., 2007, 37(3): 329-32.

[18] S.S. Krishna, Formulationn of control the release of ibuprofen usingmucoadhesive tablet, Asian J. Pharm. Sci., 2006, 1 (7): 54-9

[19] R. Canaparo, A specific method for the simultaneous determination of S-(+) Ibuprofen and R-(-) Ibuprofen enantiomers in human plasma, Department of Electronics Polytechnic of Torino, Torino, Italy, 2000: 219-116.

[20] M. Rafece., Need For controlled release formulations of ibuprofen tablet, Drug Dev. and Ind. Pharmacy, 1999, 21: 1193-202.

[21] Monographs and appendix, In: Indian Pharmacopeia, Govt. of India, Ministry of Health and Family Welfare, Indian Pharmacopeia Commission, Gaziabad, 2007; Vol – 1, 2, 3: 1514 – 515.

[22] British Pharmacopeia, The Dept. of Health Society, Service and Public Safety, 2005, Vol (3): 2703.