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Formulation, Development, And Evaluation Of A Nonsteroidal Anti-Inflammatory Drug's For Bilayer Tablet

Sivam kumar[1], Firoz khan[2], Kailash kumar Pathak[3], Deepak Verma[4], Nida Faheem[5]

Faculty of Pharmacy, SSSUTMS

Abstract:
The prepared tablets were evaluated for pre-compression and post compression parameters.The loose bulk density (LBD) and Tapped bulk density (TBD) of the powders of different formulations were evaluated before the compression of powders in to tablets.
The results of the Compressibility index of all the formulations ranges from 22.455% to 25.176%. Results clearly showed that the flow ability of all the formulations was good and also the powder had good compressibility. The thickness depends on the size of the punches (8 mm) and the weight of one tablet (150mg). The value of thickness ranges between 2.1±0.3 to 2.6±0.2mm.The results of friability test indicate that the tablet possesses good mechanical strength. The friability value ranges from 0.621±0.024 to 0.853±0.015.The values of tablets average weight ranging from 145±5 to 154±3mg. All the tablets passed weight variation test as the % weight variation was within the USP Pharmacopoeia's limits of ±5% of the weight.

Key words: Tablet, Bylayertablet, Nicotinamide, Aspirin.

Introduction:

Aspirin is a non-steroidal anti-inflammatory agent which is prescribed to alleviate mild to moderate pain. Besides analgesics property, aspirin also has anti- inflammatory property, antipyretic property as well as platelet aggregation inhibition effect. Aspirin can inhibit directly and irreversibly the enzyme cyclooxygenase, both COX-1 and COX-2 to decrease the production of prostaglandins and thromboxanes from arachidonic acid. Other NSAIDS such as ibuprofen and diclofenac sodium are reversible cyclooxygenase inhibitors (1,2).
It is frequently used to treat pain and inflammation in patients with osteoarthritis and rheumatoid arthritis (3). Additionally, it demonstrated remarkable effectiveness in managing perioperative and postoperative pain related to gynecological, orthopedic, abdominal, and dental surgeries in a number of clinical trials (2). However, lornoxicam's short half-life of three to five hours limits its usefulness (4, 5). Furthermore, lornoxicam exhibits a clear pH-dependent solubility that is marked by extremely poor solubility in the stomach's acidic environment (5). As a result, it stays in contact with the stomach wall for an extended amount of time, which may cause local irritation and ulceration (6). It is frequently used to treat pain and inflammation symptoms in Controlled-release formulations have been developed using the layered tablet concept (7–12). A fast-release layer combined with single (7–10) or double sustained-release layers typically make up such a tablet, which is regarded as a biphasic delivery system that is intended to release the medication at two different rates (11,12). Conventional controlled-release dosage forms typically do not offer a quick onset of action following oral administration and instead delay the release of medications (13, 14). Because the drug is rapidly released from the fast-release layer, the drug plasma concentration rises quickly, and the drug release from the sustained-release layer continues, the layered tablets provide a pharmacokinetic advantage over traditional controlled-release dosage forms

(14). This release pattern, which is followed by a sustained-release phase to prevent repeated drug administration, is necessary for effective treatment in many therapies, especially when maximum relief must be obtained as soon as possible. According to reports, NSAIDs are good candidates for this kind of administration (13, 14).

Material and methods

Drug: Nicotinic Acid & Aspirin

Preformulation studies

Preformulation investigations are designed to deliver all necessary data especially physicochemical, physico-mechanical and bio pharmaceutical properties of drug substances, excipients and packaging materials [17,18].

Organoleptic properties

Organoleptic properties of the drug substance are very important for designing the dosage form. The colour, odour and tests of the drug are characterized.

Solubility Analysis

An important Physical-chemical property of a drug substance is solubility, especially aqueous solubility [19]. A drug must possess some aqueous solubility for therapeutic efficacy in the physiological pH range of 1 to 8. For the determination of solubility of Nicotinic acid and Aspirin in various solvents that were methanol, ethanol, chloroform and distilled water etc. 5mg of each drug was added to 10 ml of each solvent in a test tube and shaken for few minutes at room temperature (21.0 ± 1.5°C).

Loss on drying (%)

Loss on drying is the loss of weight expressed as percentage w/w resulting from water and volatile matter of any kind that can be driven off under specified conditions [20].

Loss on drying is directly measured by IR moisture balance. Firstly calibrated the instrument by knob, then taken 5 gram of sample (powder) and fixed the temperature at 100°C to 105°C for 15 minutes and constant reading, and fixed the knob and check percent moisture.

Melting point

Melting point of Nicotinic acid and Aspirin was determined using open capillary method by melting point apparatus [21].

Determination of UV-visible absorption maxima of Nicotinic acid and Aspirin

Preparation of calibration curve of Nicotinic acid in 0.1 N HCl: 10mg of Nicotinic acid was engaged in 10ml volumetric flask and dissolved upto 10ml with 0.1N Hydrochloric acid to contribute the concentration of 1000 □g/ml. 1ml of beyondwas diluted to 10ml with 0.1 N HCl to give concentration of 100□g/ml. From the beyond stock solution, aliquots of 0.5, 1.0, 1.5, 2.0 and 2.5 ml were shifted to 10 ml volumetric flasks and made up to the mark with 0.1 N HCl. This solution was perused in UV- Visible Spectrophotometer.Sample was subjected to scan with a wavelength range of 200.0 to 400.0 with fast scan speed. The absorbance of these and a graph of concentration versus absorbance was plotted.

FTIR spectroscopy of Nicotinic acid and Aspirin

The purity of pure drug was determined by I.R. Approximately 10 mg of Nicotinic acid and Aspirin

was triturated with 100 mg of dried potassium bromide(KBr) in agatte mortar. Pellet was prepared by using KBr press pellet method. Pellet was scanned between the ranges of 400 to 2000 cm^{-1} with background correction[22]. The spectrum was recorded and major peaks were determined.

Formulation development of bilayer tablet by direct compression

The term "direct compression" is defined as the process by which tablets are compressed directly from powder mixture of API and suitable excipients. No pretreatment of the powder blend by wet or dry granulation procedure is required.

Preparation of instant layer of Aspirin (Phase-1)38

Fast dissolving (Instant Layer) tablets of Aspirin were prepared by direct compression method after incorporating different super disintegrants such as, crosscarmellose sodium (Ac-Di-Sol), crospovidone and sodium starch glycolate in different concentrations. The ingredients given below were weighed and mixed in geometric progression in a dry and clean mortar. Then the ingredients were passed through mesh #60.

Each tablets weighing 350mg, were obtained.

Table 1: Composition of Aspirin fast dissolving tablets

Ingredients(mg)	Formulation code								
	IF1	IF 2	IF 3	IF 4	IF 5	IF 6	IF 7	IF 8	IF 9
Aspirin	75	75	75	75	75	75	75	75	75
Sodium Starch Glycolate	10	20	30	-	-	-	-	-	-
Croscarmellose Sodium	-	-	-	10	20	30	5	10	15
Crospovidone	-	-	-	-	-	-	5	10	15
Microcrystalline Cellulose	50	40	30	50	40	30	50	40	30
Talc	5	5	5	5	5	5	5	5	5
Magnesium Stearate	10	10	10	10	10	10	10	10	10
Total weight	150	150	150	150	150	150	150	150	150

Evaluation of Precompression Parameter

Bulk density: Both loose bulk density (LBD) and tapped bulk density (TBD) were determined

Carr's Compressibility index: Percent compressibility of powder mix was determined by Carr's compressibility index, calculated by using following formula:-

Table 2: Grading of the powders for their flow properties according to Carr's Index

S. No.	Carr's Compressibility index	Flow
1.	5 – 15	Excellent
2.	12 – 16	Good
3.	*18 – 21	Fair to passable
4.	*23 – 35	Poor
5.	33 – 38	Very poor
6.	>40	Very very poor

***Adding glidant e. g. Talc should improve the flow properties**

Evaluation of post compression parameter

Shape and colour of tablets:
Thickness test 40
Weight variation test

Twenty tablets were selected randomly from each formulation and average weight was determined. The tablets were weighed individually and compared with average weight. The U.S Pharmacopoeia allows a little variation in the weight of a tablet.

Table 3: Percentage deviation in weight variation

S. No.	Average weight of a tablet	Percentage deviation
1.	130 mg or less	10
2.	More than 130 mg and less than 324 mg	7.5
3.	324 mg or more	5

In all the formulations the tablets weight is more than 324 mg, hence 5% maximum difference allowed.

Hardness test

The hardness of tablet was measured by Pfizer hardness tester and results were expressed in Kg/cm^2.

Friability test

For this, 20 tablets were taken from each formulation and the friability was determined using Roche friabilator. The equipment was run for 4min at 25 revolutions per minute[41]. The tablets were taken out, dedusted and reweighted and % friability was calculated. The friability was determined as the mass loss in percent according to Equation:-

The test complies if tablets not loose more than 1% of their weight

Uniformity of drug content:

The test is mandatory for tablets with 10mg or less weight of active ingredient. Ten randomly

selected tablets from each formulation (F1 to F9) were finely powdered and Drug

Method for preparation of Nicotinic acid sustain release tablets
Direct compression was followed to manufacture the matrix tablets of Nicotinic acid.

Evaluation of tablets
All the tablets were evaluated for following different parameters which includes;
General Appearance, Thickness and diameter, Drug content, Hardness, Friability, Uniformity of weight, Dissolution rate studies.23

Evaluation of bilayer tablets 24
All the tablets were evaluated for following different parameters which includes;

General Appearance , Thickness and diameter Hardness, Friability, Uniformity of weight , Drug content ,Dissolution rate studies.

RESULTS AND DISCUSSION
Results of preformulation study
Organoleptic characteristics

Table 4: Organoleptic characteristics of Nicotinic acid and Aspirin

S. No.	Properties studied	Nicotinic acid	Aspirin
1.	Colour	White crystalline powder	White crystalline powder
2.	Odour	Odorless	Odorless
3.	Taste	Bitter	Bitter

Solubility determination

Table 5: Solubility determination of Nicotinic acid and Aspirin

Solvents	Solubility of Nicotinic acid	Solubility of Aspirin
Methanol	Slightly soluble	Freely soluble
Ethanol	Slightly soluble	Freely soluble
Distilled water	Slightly soluble	Soluble
Phosphate buffer pH 6.8	Freely soluble	Sparingly soluble
0.1 N HCl	Freely soluble	Soluble
0.1 N NaOH	Soluble	Sparingly soluble

Solubility of Nicotinic acid was examined that soluble in 0.1 N NaOH, Slightly soluble in methanol, ethanol , distilled water, and freely soluble in phosphate buffer pH 6.8 and
0.1 N HCl. The solubility of Aspirin was examined freely soluble in methanol and ethanol, sparingly soluble in phosphate buffer pH 6.8, and 0.1 N NaOH, soluble in
0.1 N HCl and distilled water.
Results of loss on drying
Results: Results of loss on drying of Nicotinic acid and Aspirin were found to be 0.274±0.005%

and 0.352±0.002%.

Results of melting point of Nicotinic acid and Aspirin

Table 6: Results of melting point

S. No.	Melting point of Nicotinic acid	Melting point of Aspirin
1.	234-237°C	134-136°C

Results of melting point of Nicotinic acid and Aspirin were found to be 234-237°C and 134-136°C respectively.

Calibration curve of Nicotinic acid and Aspirin

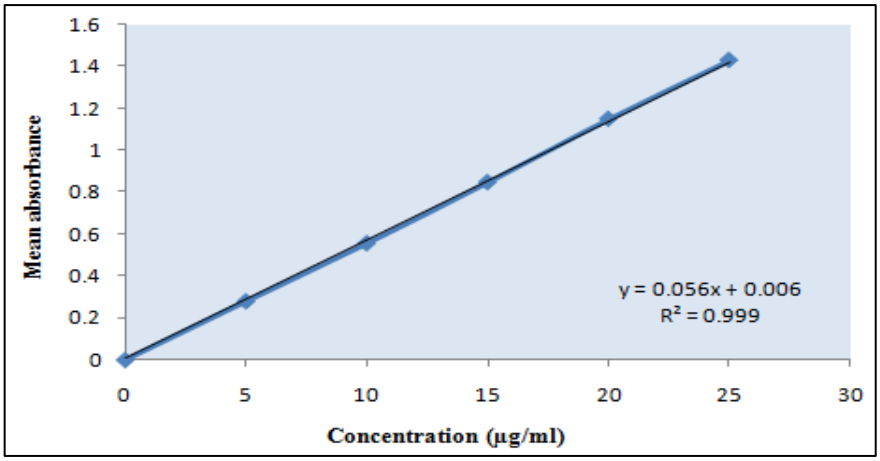


Figure 1: Calibration curve of Nicotinic acid

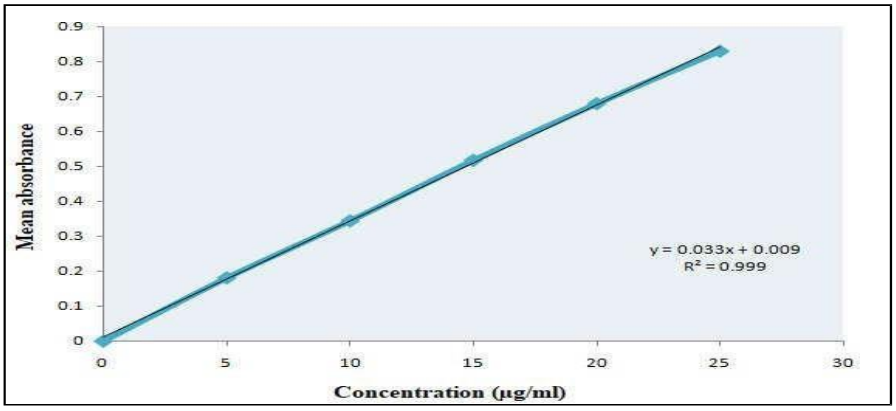


Figure 2: Calibration curve of Aspirin

7.1.3 FTIR spectra of Nicotinic acid and Aspirin

Infra- red spectrum is an important record which gives sufficient information about the structure of a compound. This technique provides a spectrum containing a large number of absorption band from which a wealth of information can be derived about the structure of an organic compound. The region from 0.8 µ to 2.5 µ is called Near Infra-red and that from 15 µ to 200 µ is called Far infra-red region. Approx 5 mg of drug was mixed with KBr and prepared their pallet. Pallet was analyse using FT-IR spectrophotometer (Bruker, USA).

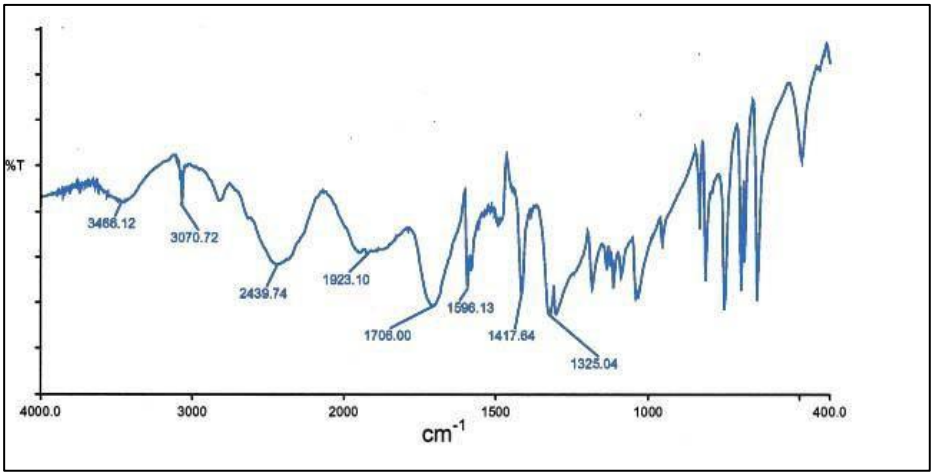


Figure 3: FTIR spectra of Nicotinic acid

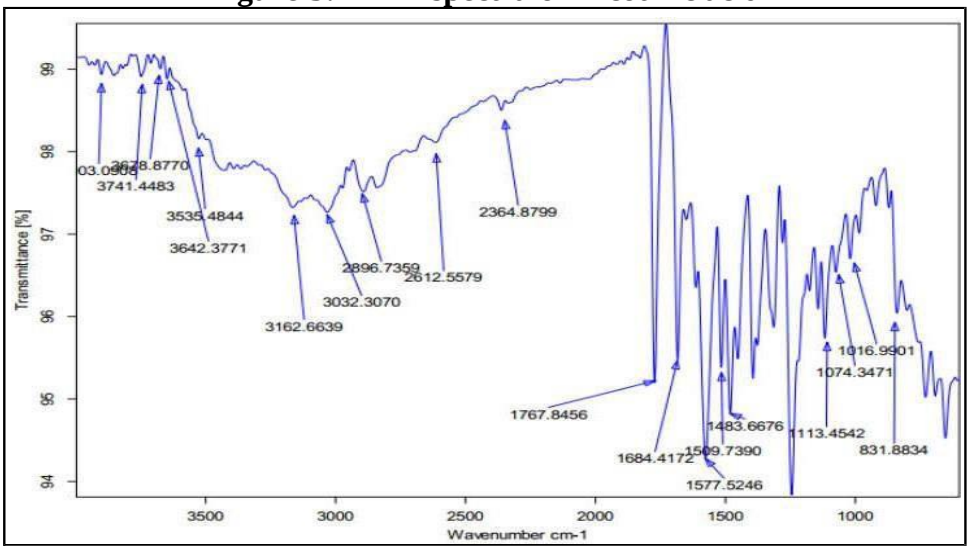


Figure 4: FTIR spectra of Aspirin

Results of pre-compressional parameters of instant release layer of Aspirin The loose bulk density (LBD) and Tapped bulk density (TBD) of the powders of different formulations were evaluated before the compression of powders in totablets. The bulk density and the tapped density for all the formulations varied from

0.319 to 0.357 gm/cm^3 and 0.424 to 0.464 gm/cm^3 respectively.

The values obtained lies within the acceptable range. The difference exists between the bulk density and tapped density found to be very few. This result helps in calculating the % compressibility of the powder.

The result of Hausner's ratio of all formulations ranges from 1.290 to 1.345. Results of Hausner's ratio of all formulations were shown in Table no 7.6 which indicatesthat the flow ability of all the formulation.

The results of the Compressibility index of all the formulations ranges from 22.455% to 25.175%. Results of Compressibility index of all the formulations were shown in the Table no 7.6. Results clearly showed that the flow ability of all the formulations was good and also the powder had good compressibility.

Table 7: Results of pre-compressional parameters of Aspirin

Formulation code	Parameters			
	Loose Bulk density(gm/ml)	Tapped bulk density(gm/ml)	Carr's Index (%)	Hausner's Ratio
AF1	0.324	0.431	24.768	1.329
AF2	0.346	0.456	24.671	1.328
AF3	0.353	0.461	23.378	1.305
AF4	0.357	0.464	23.111	1.301
AF5	0.346	0.457	24.237	1.320
AF6	0.336	0.431	22.455	1.290
AF	0.31	0.42	25.17	1.33
AF8	0.324	0.432	24.595	1.326
AF9	0.327	0.439	25.572	1.345

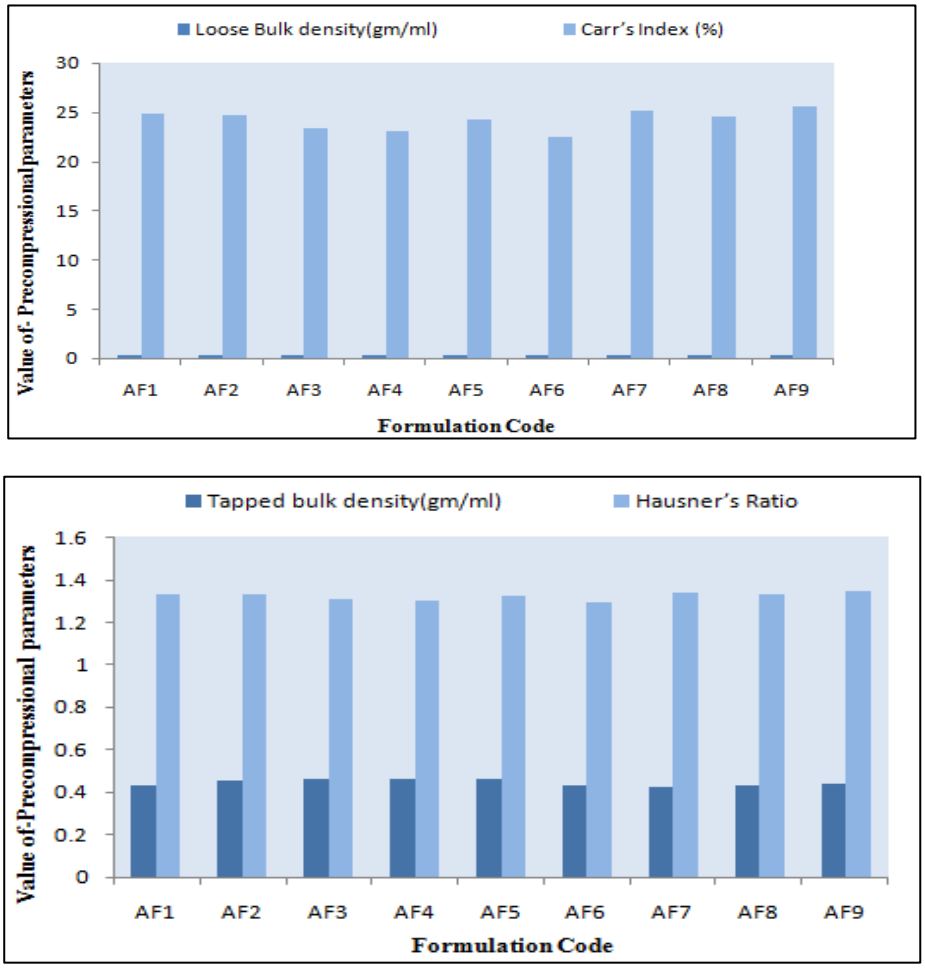


Figure 6: Graphical representation of results of pre-compressional parameters of Aspirin

Results of post-compression parameters of all formulations

Thickness

The thickness of the tablets was reported in the micrometer (mm).The thickness of tablet indicates that, die fill was uniform. The thickness depends on the size of the punches (8 mm) and the weight of one tablet (150mg). The value of thickness ranges between 2.1±0.3 to 2.6±0.2mm.

Friability

Friability determines the strength of the tablets. The friability for all the formulations was below 1% indicating that the friability was within the prescribed limits. The results of friability test indicate that the tablet possesses good mechanical strength. The friability value ranges from 0.621±0.024 to 0.853±0.015.

Hardness

The mean hardness values were measured for all the formulation using Monsanto hardness tester. The hardness value ranges from 3.2±0.3 to 3.6±0.2kg/cm^2.

Uniformity of weight

Twenty tablets were randomly selected from each formulation and evaluated The obtained data

were almost uniform. The values of tablets average weight rangingfrom 145±5 to 154±3mg. All the tablets passed weight variation test as the % weight variation was within the USP Pharmacopoeia's limits of ±5% of the weight.

Drug content

The % drug content of all the formulated tablets were found within the limit. % drug content value of drug was within 98.64±0.15% to 99.86±0.25%.The results within the range indicate uniform of mixing.

Table 8: Results of post-compression parameters of all formulations

F. Code	Hardness test (kg/cm^2)	Friability (%)	Weight variation (%)	Thickness (mm)	Drug content (%)
AF1	3.5±0.2	0.659±0.045	149±3	2.2±0.2	98.85±0.32
AF2	3.2±0.3	0.653±0.023	150±4	2.1±0.3	98.74±0.25
AF3	3.4±0.2	0.712±0.014	152±5	2.3±0.2	98.64±0.15
AF4	3.5±0.1	0.621±0.027	145±5	2.4±0.1	98.85±0.26
AF5	3.5±0.2	0.718±0.032	152±3	2.5±0.2	99.05±0.32
AF6	3.4±0.3	0.621±0.024	148±2	2.5±0.1	98.65±0.14
AF	3.6±0.	0.853±0.0	152±	2.6±0.	99.86±0.
AF8	3.4±0.1	0.753±0.032	148±5	2.4±0.2	98.85±0.36
AF9	3.4±0.2	0.684±0.035	154±3	2.3±0.2	98.75±0.15

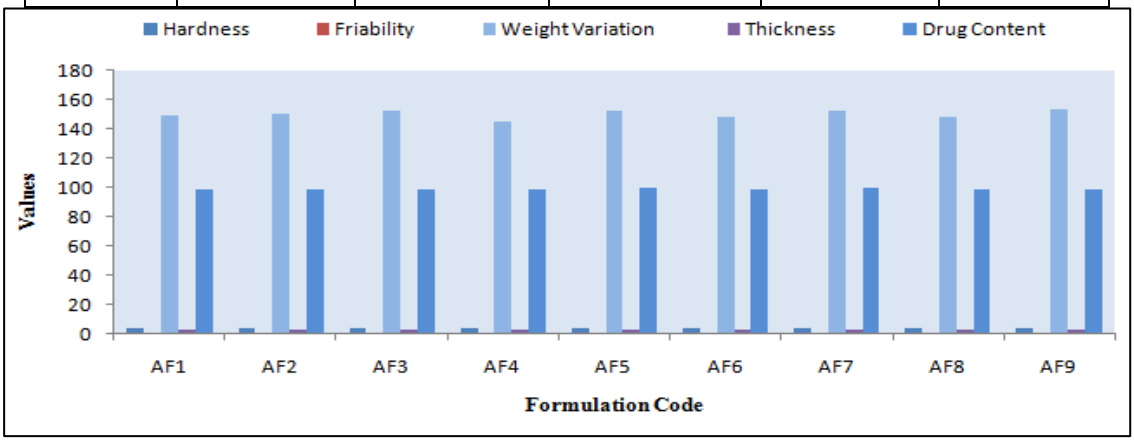


Figure 7 : Graphical representation of post-compression parameters

Results of disintegration time of instant layer of Aspirin

Disintegration time of formulation AF1, AF2, AF3, AF4, AF5, AF6, AF7, AF8 and AF9 wasfound to be 88±3, 84±2, 85±6, 97±5, 88±4, 87±3, 39±2, 45±5 and 48±4 sec.

respectively. The Minimum Disintegration time was found in formulation IF7 (39±2), select as

optimized formulation for instant layer of aspirin.

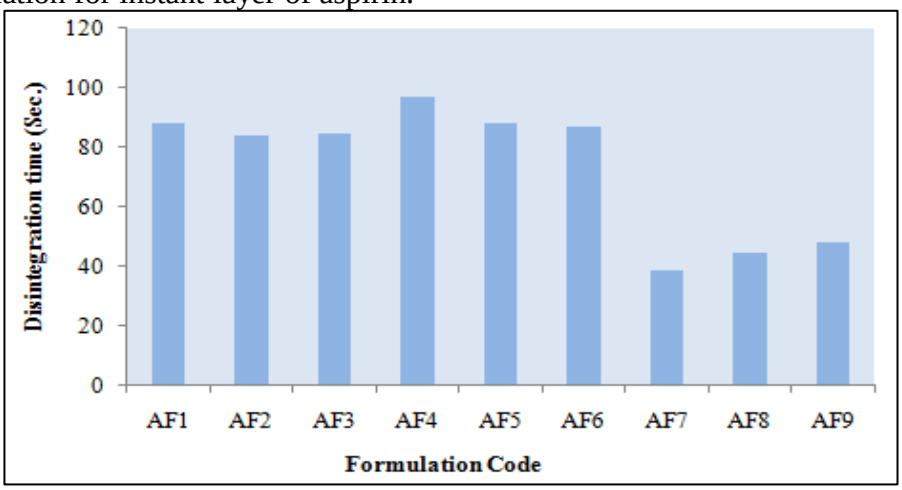


Figure 8 : Graphical representation of disintegration time

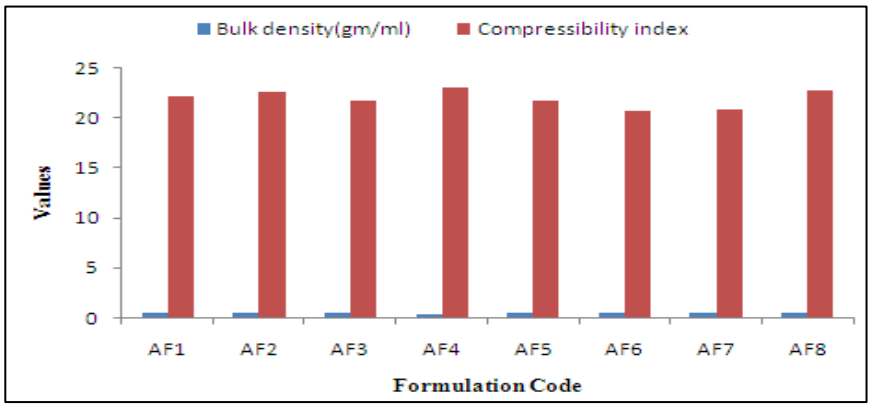
Formulation of Nicotinic acid matrix tablets

The loose bulk density (LBD) and Tapped bulk density (TBD) of the powders of different formulations were evaluated before the compression of powders in to tablets. The bulk density and the tapped density for all the formulations varied from 0.364 to 0.396 gm/cm^3 and 0.474 to 0.498 gm/cm^3 respectively.

The values obtained lies within the acceptable range. The difference exists between the bulk density and tapped density found to be very few. This result helps in calculating the % compressibility of the powder.

The result of Hausner's ratio of all formulations ranges from 1.262 to 1.302. which indicatesthat the flow ability of all the formulation.

The results of the Compressibility index of all the formulations ranges from 20.684% to 23.159%. Results of Compressibility index of all the formulations .Results clearly showed that the flow ability of all the formulations was good and also the powder had good compressibility.



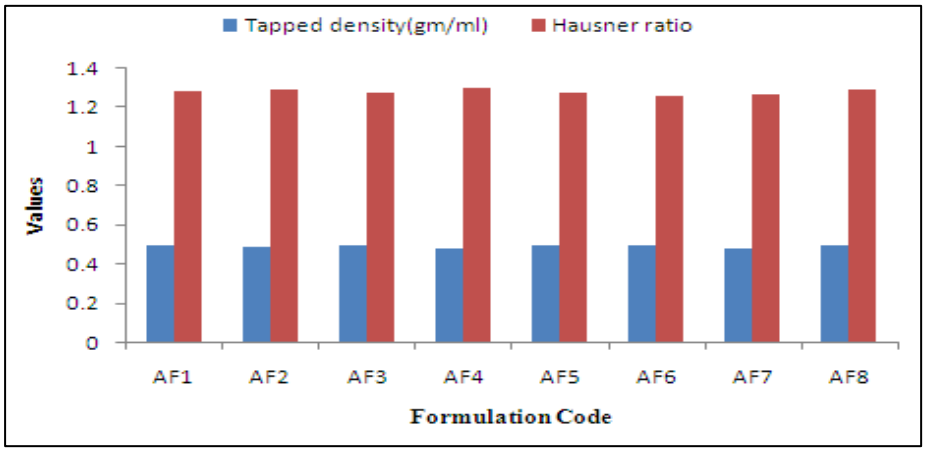


Figure 9: Graphical representation of pre-compression properties of Nicotinic acid tablets

Results of post compression properties of sustain release tablets of Nicotinic acid

Thickness

The thickness of the tablets was reported in the micrometer (mm).The thickness of tablet indicates that, die fill was uniform. The thickness depends on the size of the punches (8 mm) and the weight of one tablet (150mg). The value of thickness ranges between 3.4 to 5.5 mm.

Friability

Friability determines the strength of the tablets. The friability for all the formulations was below 1% indicating that the friability was within the prescribed limits. The results of friability test indicate that the tablet possesses good mechanical strength. The friability value ranges from 0.488 to 0.857.

Hardness

The mean hardness values were measured for all the formulation using Monsanto hardness tester . The hardness value ranges from 5.1 to 5.5 kg/cm^2.

Uniformity of weight

Twenty tablets were randomly selected from each formulation and evaluated. The obtained data were almost uniform. The values of tablets average weight ranging from 496 to 505 mg. All the tablets passed weight variation test as the
% weight variation was within the USP Pharmacopoeia's limits of ±5% of the weight.

Drug content

The % drug content of all the formulated tablets were found within the limit. % drug content value of drug was within 98.88 % to 99.85 %.The results withinthe range indicate uniform of mixing.

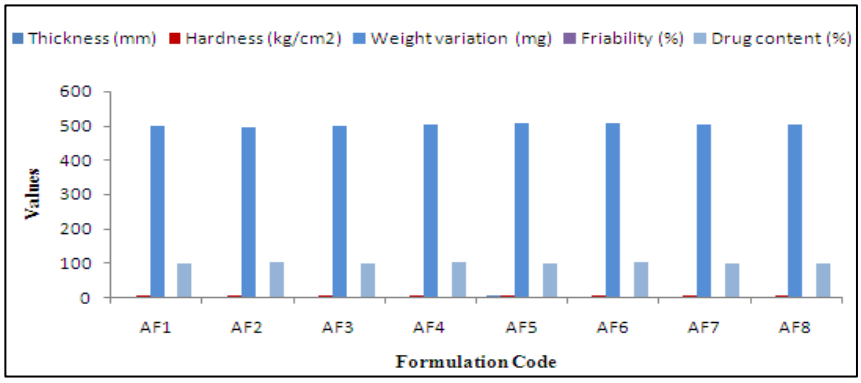


Figure 10: Results of post compression properties of Nicotinic acid tablets

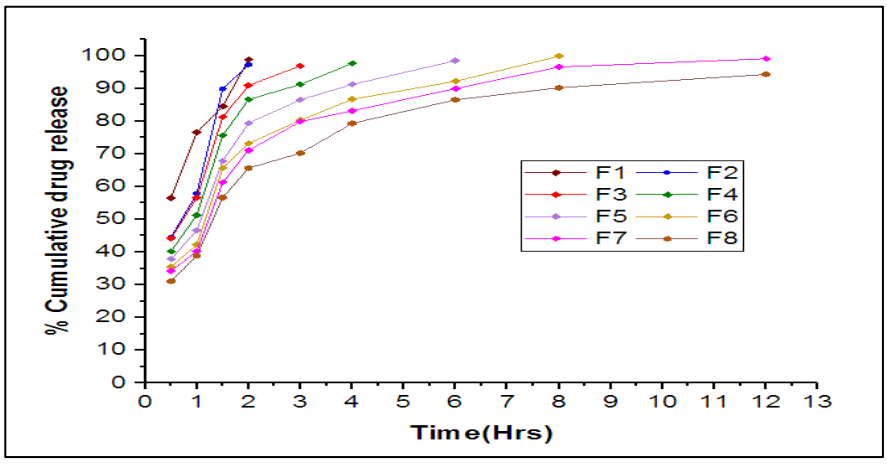


Figure 11: Graph of *in-vitro* drug release study of control layer

Results of formulation development of bilayer tablet

Table 9: Post-compression parameters of optimized formulation

Formulation	Hardness test (kg/cm^2)	Friability (%)	Weight variation	Thickness (mm)
1.	5.9	0.652	Passes	4.85

Table 10 : Results of Drug content analysis

Formulation	Aspirin (% Label Claim)	Aspirin (% Label Claim)
In-house Bilayer tablet	99.45	99.85

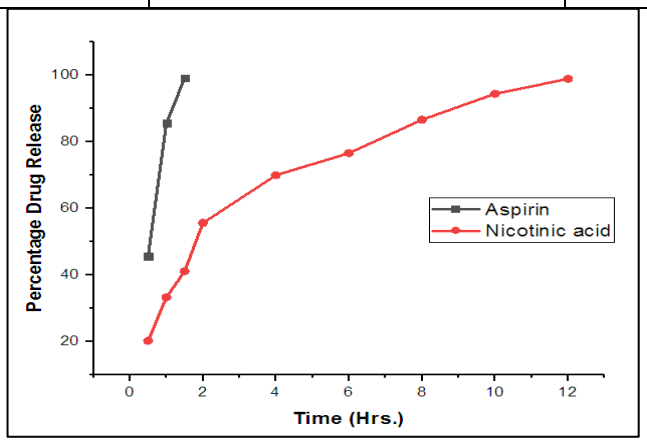


Figure 12 : Graph of release of bilayer tablets

A dissolution study shows the release of Aspirin and Nicotinic acid. The Instant layer of Aspirin release approx 99.12 percent drug within 1.5 Hrs. and control layer Nicotinic acid shows release up

to 12 Hours Approx 98.95 percent of drug release in 12 hours.

Conclusion

Fast-dissolving (instant layer) tablets of aspirin were successfully formulated by the direct compression method using different superdisintegrants, including croscarmellose sodium, crospovidone, and sodium starch glycolate at various concentrations. Pre-compression evaluation of the powder blends showed acceptable loose bulk density and tapped bulk density values, indicating good packing characteristics. The Hausner's ratio and compressibility index values confirmed that all formulations possessed good flowability and compressibility, making them suitable for direct compression.

Post-compression evaluation demonstrated that all tablet formulations complied with pharmacopeial standards. Uniform tablet thickness indicated consistent die filling during compression. Friability values below 1% confirmed adequate mechanical strength, while hardness values were within an optimal range, ensuring both tablet integrity and patient handling convenience. Weight variation results further confirmed uniformity of dosage, as all formulations met USP requirements.

Overall, the results indicate that the direct compression technique is a suitable and effective method for the preparation of fast-dissolving aspirin tablets. The use of superdisintegrants at appropriate concentrations produced tablets with satisfactory physical characteristics and acceptable quality parameters, suggesting their potential applicability for rapid drug delivery and improved patient compliance.

REFERENCES:

01. Merck & Co, Inc.The Merck index.13th ed.Whitehouse Station: Merck & Co.Inc:2001
02. Homdrum E.M, Likar R, Nell G.Xefo Rapid: novel effective tool for pain treatment. Eur Surg.2006; 38:342-52
03. Kidd B, Frenzel W.A multicenter, randomized, double blind study comparing lornoxicam with diclofenac in osteoarthritis. J Rheumatol.1996; 3:1605-11.
04. Balfour JA, Fitton A, Barradell LB. Lornoxicam. A review of its pharmacology and therapeutic potential in management of pain and inflammatory conditions.Drugs.1996:51:639-57
05. Skjoodt NM, Davies NM. Clinical pharmacokinetics of Lornoxicam. A short half-life oxicam. Clin. Pharmacokinet1998; 34(6):421–428.
06. Lin SZ, Wouessidjewe D, Poelman MC, Duchene D .In Vivo evaluation of indomethancin/cyclodextrin complexes .Gastrointestinal tolerance and dermal anti-inflammatory activity. Int. J Pharm.1994; 106; 63-7.
07. CN Kumar AB, Pandit HK, Singh SP , Design and evaluation sustained release bilayer tablets of propranolol hydrochloride, Acta Pharm. 2007; 57, 479–489.
08. Uekama K. Matsubara K, Abe K, Horiuchi Y, Utility of beta cyclodextrin; Cellulose derivative combination as modified-release drug carrier. J. Pharm Sci. 1990; 79:244-8.
09. Wang Z. Horikawa T. Hirayama F, Uekama K. Design and in vitro evaluation of modified release oral dosage form of nifidifine. J. Pharm Pharmacol.1993; 45:942-6. 10)
10. Kumar A. Agrawal SP, Khanna R. Modified released bi-layered tablet of melatonin using betacyclodextrin.Phamazie.2003; 58:642-4
11. Yan G, Li H, Zhang R. Prepration and evaluation of a sustained –release formulation of nifedipine HPMC tablets .Drug Dev Ind Pharm.2000;26:681- 6.
12. Fassihi RA, Ritschel WA. Multiple – layer, directcompression controlled release system: in vitro and in vivo evaluation .J Pharm Sci 1993; 82:750-4
13. Lopes CM, José M. Lobo S, Pinto F, Costa PC. Compressed Matrix Core Tablet as a Quick/Slow

Dual-Component Delivery System Containing Ibuprofen, AAPS Pharm SciTech 2007; 8 (3) 76.
14. Maggi L, Machiste EO, Torre ML, Conte U. Formulation of biphasic release tablets containing slightly soluble drugs. European journal of pharmaceutics and biopharmaceutics, 1998; 48, 37- 42.
15. Girish SS , Devendra KJ , Dhananjay MM .Prepration and in vitro evaluation of bilayer and floating-bioadhesive tablets of rosiglitazone maleate., Asian Journal of Pharmaqceutical Sciences 2007; 2 (4), 161-169.
16. Marshall K, Lachman N, Liberman HA. The theory and practice of industrial pharmacy. 3rd Ed. Mumbai, Varghese Publishing House; 1987, p. 66- 69.
17. Albert, A.A. & Serjeant, E.P. (1984). Ionization Constants of Acids and Bases. Wiley: New York, USA.
18. Yalkowiski, S.H. & Roseman, T.J. (1981), Chapter 3 Marcel Dekker, newy. In: Techniques of Solubilisation of Drugs (edited by S. H. Yalkowski).
19. Indian Pharmacopeia (2007), Vol. 4.
20. European Pharmacopoeia (2004), Vol. 1. Directorate for the Quality of Medicines of the Council of Europe (EDQM), p. 628. Page 66
21. https://www.sciencedirect.com/topics/nursing-and-health professions/melting-point
22. https://www.researchgate.net/publication/226147743_fourier_transform_infr ared_spectroscopy
23. Anilkumar S, Sachin K, et.al, Comparative evaluation of formulation design using chemically modified pectin and eudragit for sustain release nateglinide, International journal of novel drug delivery technology, 2(1), 2012, 240-247.
24. R. Prema, S. Jeevanandham, M. Sekar, T. Rajkumar, D. Dhachinamoorthi, K. B. ChandraSekhar, M. Arigala., Res. J Pharm. Bio. Chem. Res., 2010, 1(2), 70.