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Formulation Development and Evaluation of Tablet Formulation Containing Ibuprofen HCL with Castor Oil

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ABSTRACT

The purpose of this study was to formulate and evaluate conventional tablets of Ibuprofen HCl with Castor oil. Castor oil helps to overcome the hepatotoxic effect of Ibuprofen HCl. Direct compression method was used to formulate tablets, which contained Castor oil in different proportion from batch F1-F4. Formulation of tablets was prepared by the powder blend of different ratios of Castor oil to get desirable drug release profile. All batches were evaluated for flow property (Pre compression study). Evaluation parameters of formulated tablets were hardness, friability, thickness, drug content, weight variation, and the in-vitro drug release rate pattern. Results indicated that the formulation F2 was the most promising formulation as the drug release from this formulation was high as compared to other formulations. In formulation F2, percentage drug release of Ibuprofen HCl is 97.01% at 60 min.

KEYWORDS: *Ibuprofen HCl, Castor oil, Conventional tablet, NSAIDs, Direct Compression*

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INTRODUCTION

Nonsteroidal anti-inflammatory drugs (NSAIDs) are a drug class FDA-approved for use as antipyretic, anti-inflammatory, and analgesic agents. These effects make NSAIDs useful for treating muscle pain, dysmenorrhea, arthritic conditions, pyrexia, gout, migraines, and used as opioid-sparing agents in certain acute trauma cases. NSAIDs are typically divided into groups based on their chemical structure and selectivity: acetylated salicylates (aspirin), non-acetylated salicylates (diflunisal, salsalate), propionic acids (naproxen, ibuprofen, acetic acids (diclofenac, indomethacin), enolic acids (meloxicam, piroxicam) anthranilic acids (meclofenamate, mefenamic acid), naphthylalanine (nabumetone), and selective COX-2 inhibitors (celecoxib, etoricoxib).Topical NSAIDs (diclofenac gel) are also available for use in acute tenosynovitis, ankle sprains, and soft tissue injuries. It is common to use NSAIDs to ease minor and short-term inflammation and pain. Some conditions that may cause temporary pain include: arthritis, backache, cold or flu, headaches, period pain., joint or bone injuries, sprains, and strains, muscle or joint complaints, toothache If any of these problems become chronic, a person should consider the safety of using NSAIDs. NSAIDs work by preventing an enzyme (a protein that triggers changes in the body) from doing its job. The enzyme is called cyclooxygenase, or COX, and it has two forms. COX-1 protects the stomach lining from harsh acids and digestive chemicals. It also helps maintain kidney function. COX-2 is produced when joints are injured or inflamed. NSAID toxicity can manifest as GI bleeding, hypertension, hepatotoxicity, and renal damage. Ibuprofen is used to relieve pain from various conditions such as headache, dental pain, menstrual cramps, muscle aches, or arthritis. It is also used to reduce fever and to relieve minor aches and pain due to the common cold or flu. For ongoing conditions such as arthritis. Castor oil have hepatoprotective, choleretic and anticholestatic

activity. Castor oil is a promising commodity that has a variety of applications in the coming years, particularly as a renewable. energy source. It is used as a powerful laxative, A natural moisturizer, may promote wound healing, May be helpful for cleaning and storing dentures. Castor oil has no noted interactions with other drugs. Direct compression is employed to define the method by which tablets are compressed directly from powder blend of active ingredients and suitable excipients, which will flow uniformly within the die cavity and forms a firm compact.

Materials and Methods:

Ibuprofen HCl was provided by Solanki pharmaceuticals, (Pune, India). Fine Chem Ltd. (Mumbai, India) supplied Castor oil, Stearic acid, Sodium bicarbonate, Silicon dioxide, Lactose. All of the reagents used in this experiment was analytical quality grade.

Methods:

Method for Preparation of Tablets:

Dry granulation:

This method is used for tablet preparation, in case tablet ingredients are highly sensitive to moisture, or unable to with stand elevated temperatures during drying, slugging may be used to form the granules. Dry granulation or double compression, usually eliminates various steps, which involves slugging of the powder mass. The active ingredient, diluent and lubricant are blended together, to form the slug. Thus, the compressed slug is passed through the mesh or through the mill, and the remaining lubricant is added to the granulation, blended properly and compressed to form the tablets.

Direct Compression:

In which tablets formulations are directly compressed from a powder blend of suitable excipients and API is called a direct compression method. Pre-treatment of blended powder by dry necessary In this formulation. It provides merits mostly in terms of speedy production, as it requires less machinery, reduced number of personnel, fewer unit operations and significantly less processing time along with improved product stability. So, In this formulation direct compression method was used.

Identification of pure drug:

Identification of pure drug was carried out by UV-Visible spectroscopy and Fourier Transform Infra-Red Spectrophotometry scanned in the range of 200-400nm.Also Identification of pure drug was carried out by Differential Scanning Calorimetry (DSC) study.

Drug-excipient compatibility study:

Studies of drug-excipient compatibility are important to ascertain drug and excipients are compatible with each other. Differential Scanning Calorimetry (DSC) study and are used to study drug-excipient compatibility.

UV-Spectroscopy:

The stock solution of Ibuprofen HCl was prepared in Methanol; UV spectrum of 10µg/ml solution of Ibuprofen HCl was taken to determine its absorption maxima (λ max). The dissolved Ibuprofen Hydrochloride showed an absorbance maximum (λmax) at 224 nm. The linearity of the responses of both drugs was verified at 2–12 µg/ml concentrations. The calibration curve was obtained by plotting the absorbance versus the concentration data and was treated by linear regression analysis. The equation of the linearity curve for Ibuprofen HCl obtained was y = 0.0806x + 0.0089. The linearity curve was found to be linear for mentioned concentrations (the correlation coefficient (r^2) of determination was 0.9996 (Fig.1).

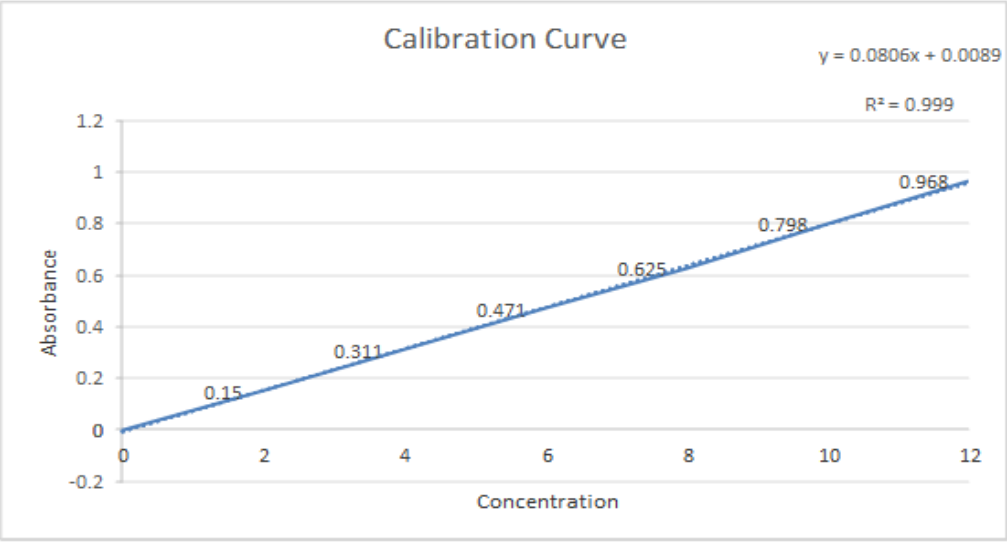

Fig.1 UV Calibration Curve of Ibuprofen Hydrochloride

FTIR spectroscopy:

FTIR (Shimadzu 8400s) spectrophotometer were used in the range of 400-4000 cm-^{1} using potassium bromide discs (Mixing ratio1:1) The samples were hermetically sealed in aluminum pans and heated at a constant rate of 10°C/ min over a temperature range of 40 to 300°C. The FTIR spectrums of pure drug Ibuprofen HCl were studied. It was observed that there were no major shifts in the main peaks of drug Ibuprofen HCl. This indicates that drug Is In pure form. Ibuprofen HCl had peaks at 3325.29 (O-H stretching), 2870.17 (C-H3 stretching), and 1712.85 (C=O stretching), 1512.24 (C=C stretching) **(Fig.2).**

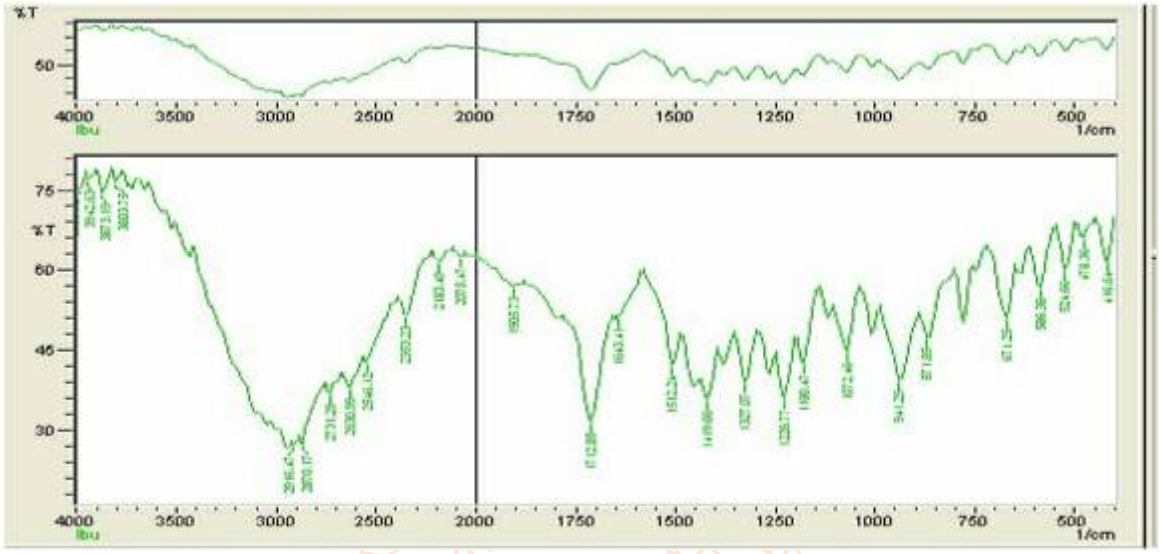

Fig.2 IR Spectrum of Ibuprofen Hydrochloride

Differential Scanning Calorimetry (DSC) study:

Mettle Toledo (*SW920) Differential Scanning Calorimeter using aluminum pans equipped with an intracooler and a refrigerated cooling system was used to analyses the thermal behavior of Ibuprofen HCl, Indian standard was used to calibrate the DSC temperature. The thermal behavior of hermetically sealed samples heated at 10˚C/min.

DSC Thermogram of Ibuprofen HCl is shown in **Fig.3** Thermogram indicates a sharp endotherm at **78.97˚C**, which is corresponding to the melting point of Ibuprofen HCl. From this it is conclude that the given sample of Ibuprofen HCl is in pure form.

Compatibility studies were performed in order to confirm the drug-excipient compatibility. The physical mixtures of Ibuprofen HCl +Castor oil and other excipients, were taken as 1:1 ratio. DSC Thermogram of given sample of Ibuprofen HCl **+**Castor Oil and other excipients is shown in **Fig 4.** Thermogram indicates a sharp endotherm at 80°C, which is corresponding to the melting point of Ibuprofen HCl. From this it is conclude that the given sample of Ibuprofen HCl+ Castor oil and other excipients is compatible with each other.

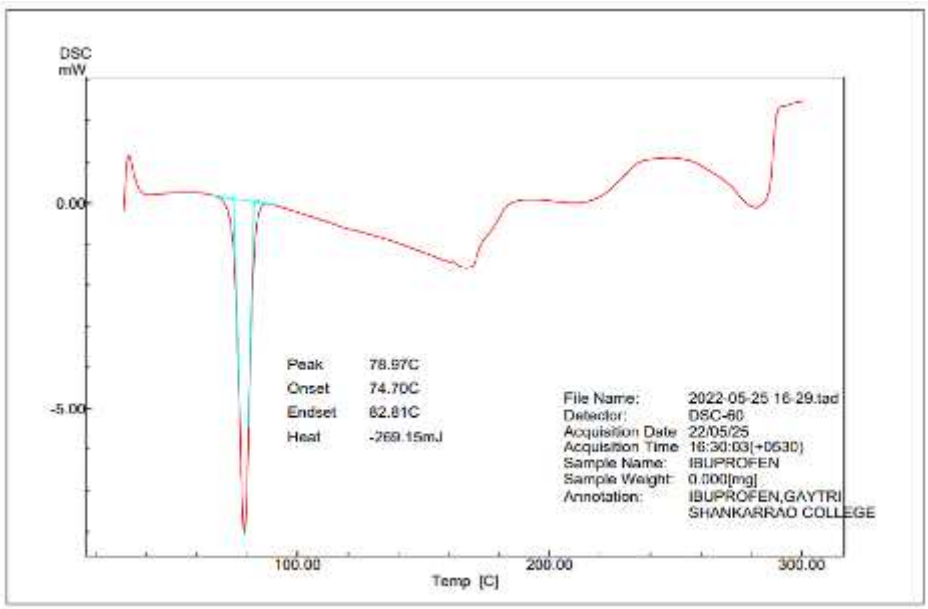

Fig.3 DSC Thermogram of Ibuprofen hydrochloride

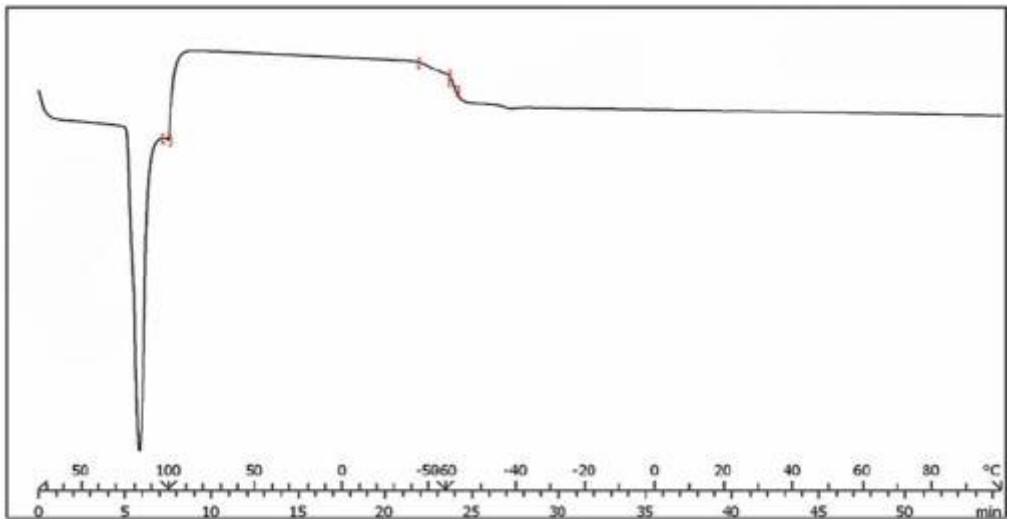

Fig.4 DSC Thermogram of Physical Mixture of Ibuprofen Excipient

Formulation of tablet:

Formulation of tablet blend for Tablets of Ibuprofen HCl. The tablet blends for different batch formulation(F1-F4) are prepared and further studied for Pre-compression properties and subjected for tablet punching by direct compression.

Table.1 Formulation of Tablet Batches (500 mg).

Sr. No.	Ingredients	Batch F1(mg)	Batch F2(mg)	Batch F3(mg)	Batch F4(mg)
01	Ibuprofen HCl	400	400	400	400
02	Castor oil	20	40	60	80
03	Stearic acid	06	06	06	06
04	Sodium bicarbonate	02	02	02	02
05	Lactose	68	48	28	08
06	Silicon dioxide	04	04	04	04

Results:

Precompression study:

Evaluation of prepared tablet blends for pre compression study:

The mass-volume relationship characteristics of a mixed blend were determined by characterization. Angle of repose, bulk density, and tapped density were all examined, with Hauser's ratio and compressibility index given in **Table.2**

Table.2 Flow Properties of Ibuprofen Hydrochloride Blend

Test	F1	F2	F3	F4
Bulk Density	0.4761 ± 0.002	0.4821 ±0.006	0.450 ±0.003	0.465 ± 0.002
Tapped Density	0.5333 ± 0.006	0.5284 ±0.002	0.502 ±0.008	0.523 ± 0.003
Compressibility Index	10.725 ± 0.40	8.8460 ± 0.30	10.35 ± 0.44	11.08 ± 0.20
Hausner's Ratio	1.120 ± 0.02	1.096 ± 0.03	1.11 ± 0.04	1.12 ± 0.03
Angle of repose	19.87 ± 0.4	19.02 ± 0.2	17.98 ± 0.4	19.65 ± 0.1

Results are mean of three determinations

Evaluation of Tablets:

The prepared tablets subjected for weight variation, thickness, hardness, friability, drug content, In-vitro disintegrating time, In-vitro dissolution studies, Assay were carried out.

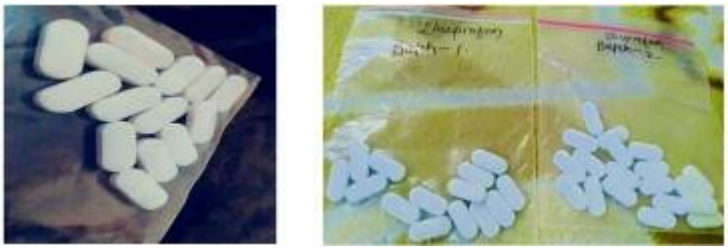

Fig.5 Formulated Ibuprofen Tablets

Table 3 Evaluations of Tablets

Batch	% Weight Variation (%w/w)	Hardness (Kg/cm^2)	Thickness (mm)	% Friability	Disintegration Time
F1	499.39 ±1.12	4.0 ± 0.3	5.1 ± 0.02	0.68 ±0.035	5 Min. 23 Sec.
F2	500.12 ±1.18	4.2 ± 0.1	5.2 ± 0.03	0.63 ±0.046	8 Min. 44 Sec.
F3	498.24 ±1.14	4.1 ± 0.4	4.9 ± 0.08	0.59 ±0.048	6 Min. 21 Sec.
F4	501.32 ±1.47	4.0 ± 0.5	5.0 ± 0.09	0.64 ±0.023	7 Min. 20 Sec.

Results are mean of three determinations

Dissolution Study

Dissolution of Formulation Batch F1-F4 for Ibuprofen hydrochloride by using dissolution test apparatus and UV Spectrophotometer.

Apparatus: - Apparatus No.2, Medium: - 900 ml of Phosphate buffer PH (7.2).

Speed and time: - 100 rpm and 60 minutes

Procedure: -

Withdraw a suitable volume of the medium and filter promptly through a membrane filter disc having an average pore diameter not greater than 1.0µm, rejecting the first few ml of the filtrate.

Dilute a suitable volume of the filtrate with the same solvent. Measure the absorbance at 224 nm of the solution of known concentration of Ibuprofen. Calculate the content of Ibuprofen HCl.imit is Not less than 75% of the stated amount of ibuprofen

Table.4 Dissolution study of Ibuprofen HCl Tablet

Time (Min)	F1 (%)	F2 (%)	F3 (%)	F4 (%)
0	0	**0**	0	0
5	5.798 ± 0.78	**6.581 ± 0.55**	6.189 ± 0.17	5.509 ± 0.51
10	13.099 ± 0.21	**15.200 ± 0.43**	14.244 ± 0.47	12.100 ± 0.11
15	25.862 ± 0.44	**41.072 ± 0.24**	33.742 ± 0.36	32.047 ± 0.52
30	60.121 ± 0.74	**64.047 ± 0.65**	54.312 ± 0.28	54.616 ± 0.63
45	79.924 ± 0.62	**85.139 ± 0.98**	84.443 ± 0.33	83.125 ± 0.47
60	88.717 ± 0.48	**97.017 ± 0.62**	94.265 ± 0.64	95.583 ± 0.12

Results are mean of three determinations

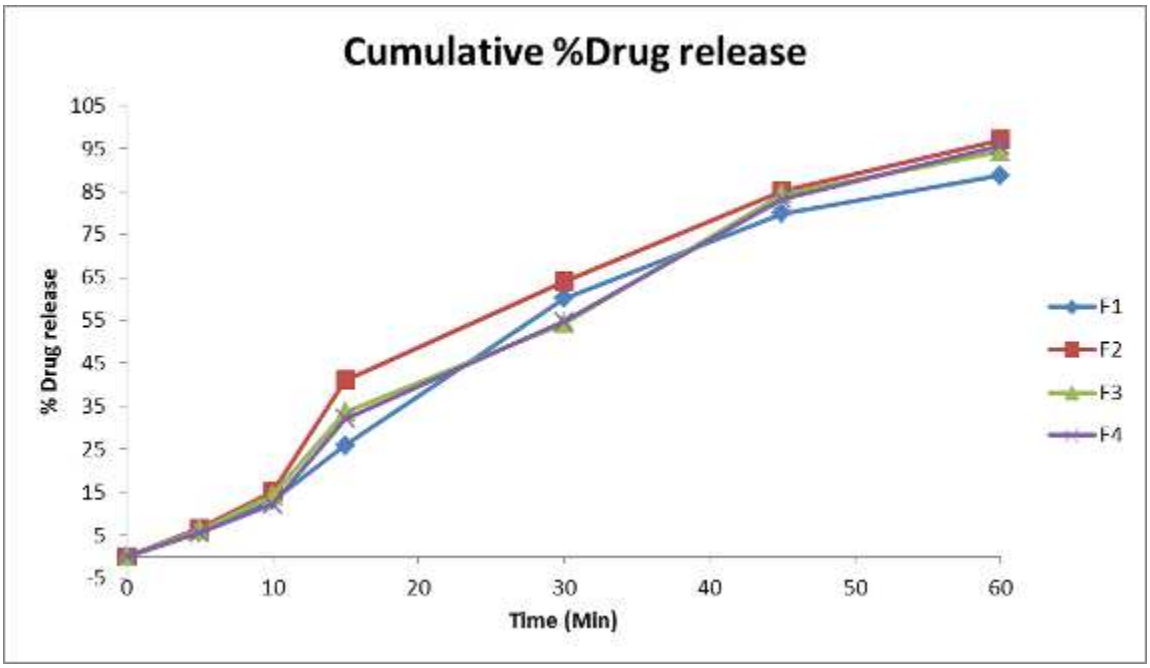

Fig.5 Cumulative In-vitro Dissolution Study

The formulation **F2** selected as a optimized formulation because of this batch showed satisfactory result of the tablets evaluation parameters. Result of in vitro % drug release profile indicated that formulation (F2) was the most promising formulations as the drug release from this formulation and assay was high as compared to other formulations. So, **F2** was found to be optimized formulation and was selected for further Assay and stability study.

Assay:
% Assay of Selected Formulation Batch F2 for Ibuprofen HCl is **101.77 %**

Stability study:
Stability study for the developed formulation F2 were carried out as per ICH guideline by storing at 40°C/75% RH up to one month. The formulation F27 was selected on the basis of their high cumulative percentage drug release. shows Cumulative percent release of F2 Formulation after three months which shows stability of formulation.

Table.5 Stability Study of Optimized Formulation F2 batch

Sr. No.	Parameter	Initial	After three months
01	Hardness	4.2	4.2
02	Thickness	5.2	5.2
03	Friability	0.19 %	0.23%
04	Weight Variation	500.12±0.10%	500.12 ±0.11%
05	Disintegration Time	8 Min 44Sec.	8 Min 59 Sec.
06	% Drug Release	98.79±0.09%	98.33±0.09 %
07	% Assay	101.77±0.12	101.20±0.1

Results are mean of three determinations

The stability study showed that the formulation F2 was physically stable when stored at 40±20°C and 75±5% RH for three months and there was no significant difference in dissolution parameters of optimized formulation.

Conclusion:
The present study was undertaken with an aim to formulate, develop and evaluate tablet of Ibuprofen with Castor oil. Preformulation study was done initially and result directed for the further course of formulation. Based on preformulation studies different batches of Ibuprofen hydrochloride was prepared using selected excipients. Powders were evaluated for tests angle of repose, bulk density, tapped density, compressibility index, and Hausner's ratio before being compressed as tablets. Various formulation of tablets of Ibuprofen hydrochloride and castor oil were developed using various concentrations of binders by dry granulation technique. The tablets were evaluated for physical observations, in vitro release study and stability studies. Observations of all formulation for physical observation had shown that, all of then comply with the specifications of official pharmacopoeias and/or standard references. Result of in vitro release profile indicated that formulation **(F2)** was the most promising formulations as the drug release from this formulation was high as compared to other formulations. The cumulative % of drug release of formulation F2 was 98.79% respectively, and % of drug assay of formulation F2 for Ibuprofen with castor oil was found 101.77±0.12%.

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