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STUDIES ON FORMULATION AND EVALUATION OF IBUPROFEN MATRIX DRUG DELIVERY SYSTEM BY USING "BEE PROPOLIS" (*APIS MELLIFERA* L.)

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Keywords:

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ABSTRACT: Ibuprofen is a Non-steroidal anti-inflammatory (NSAID) class drug and is used to treat pain, minor aches, fever, inflammation, and arthritis. Ibuprofen has an oral dose of 300 mg minimum and 3200 mg maximum in a day and is the main reason for the increase in its dosing frequency; many of the Ibuprofen formulations are of three times a day dosing and is the main reason for the development of such a formulation which can reduce the dosing frequency, so many researchers developed Ibuprofen matrix dosage form which can give a prolonged therapeutic effect. But in this formulation, Ibuprofen is combined with a Natural, Resinous substance known as "Bee Propolis" or simply "Propolis" Propolis is a natural substance collected by some species of Honey bees; it is a resinous, gummy material that has many therapeutic properties and can also be used as a natural binder in the dosage form due to its good binding abilities and, it can also give a positive synergistic effect when combined with Ibuprofen. In this study, the formulation was developed as a matrix dosage system in an oral tablet form with a dose of 400 mg/ tablet. Though not all honey bee species are capable of making propolis some of the honey bee species, such as "*Apis mellifera L.*", "*Apis Dorsata*", etc. in India are capable of making Propolis. Propolis has 350-500 chemical constituents which can be used in many therapeutic activities; such chemical constituents present in a single product makes it more valuable in further research.

INTRODUCTION: Ibuprofen is a Non-steroidal Anti-inflammatory class drug used to reduce fever and relieve minor pain and aches and also for arthritis and other minor aches [21, 22]. The minimum dose of Ibuprofen is 300 mg a day, and the maximum dose of Ibuprofen is 3200 mg/ day [22].

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Ibuprofen, as in tablet form, has the frequency of a minimum of three tablets a day and so, to reduce the frequency of dosing, there is a need to develop such type of dosage form which can provide a long therapeutic response in a single or twice a day dosing, so Ibuprofen matrix tablets by various excipients and polymers are formulated by many researchers.

But in this study, Ibuprofen is combined with "Bee Propolis" as a natural polymer and HPMC K 200 M as a synthetic polymer. "Bee Propolis" is a natural, resinous, gummy, sticky, and pliable substance [3, 4], so it is also called "The Bee Glue".

Propolis is as old as honey [5], it is collected and processed by honey bees, not all the honey bees are capable in making Propolis, as per the Indian scenario, in India there are five main species of honey bees and they are *Apis mellifera L.* (The European or Western Honey Bee), *Apis dorsata* (The Jiant Honey Bee or Rock Honey Bee), *Apis cerana* Indica (Indian Honey Bee) and *Apis florea* (The Dwarf Honey Bee). India is a huge and diverse country in its nature. But from these species, *Apis mellifera L.* (The European Honey Bee) was not native to India it was imported in the year 1983. "Bee Propolis" is also known for its therapeutic uses as in: -

- Analgesic [2, 3]
- Anti-Inflammatory [3, 7, 8, 9, 10]
- Anti-Bacterial [3, 9, 10, 11, 12, 13]
- Wound Healing [7, 14]
- Anti-Viral [3, 15, 16]

And many other therapeutic uses, but in India Bee Propolis is not well known. But the, researchers from various parts in India are working on Propolis now.

Propolis has a vast number of Chemical Compounds, many of the researchers claimed to have 350 to 500 Chemical Constituents in "Bee Propolis" [3, 6, 7]. a lot of chemical constituents make Propolis an important topic of research, and the main chemical compounds found in different samples of "Bee Propolis" are: -

- Galangin [3, 6, 7, 13]
- Pinocembrin [3, 6, 7, 11, 13]
- Pinobanksin [1, 3, 13, 16]
- Quercetin [3, 10, 11, 13, 14]
- Apigenin [1, 3, 11, 13]
- Caffeic Acid [3, 14]

So, in the formulation development. The Propolis is used as a natural polymer, and HPMC K 200 M is used as a synthetic polymer, and the excipients, such as Lactose, PVP K30, Talc, and Magnesium Stearate are used. Titanium Dioxide is used as a tablet coating material. By the help of design expert ® software developed by state ease the factorial design of tablet batches was developed and the *in-vitro* studies such as dissolution studies on formulation were studied, and the stability studies of the formulation were studied as per the ICH guidelines on stability studies, by the accelerated stability studies at (40°C ±2°C, 75 % RH) for 0 to 1 month and further tested for accelerated stability studies. All obtained results were compared with the standard references and were in the standard range.

The presence of 350 to 500 chemical constituents in a single product ("Bee Propolis") makes it an ideal substance to be used in the formulation and further *in-vivo* studies should be done to check the "Synergistic Effect" which on combination of "Bee propolis" with Ibuprofen and such drugs which has the same therapeutic effect of "Bee propolis" can be used in formulations and to check their increased therapeutic response further *in-vivo* studies are required.

MATERIALS AND METHODS: "Bee Propolis" were purchased from Kamboj Bee Farm, Hafizpur, Yamuna Nagar (State- Haryana, India), and Ibuprofen (API) was purchased from Thermosil Fine Chem Industries, Pune (State- Maharashtra, India), HPMC K200 M, Lactose, Magnesium Stearate were obtained from Research Fine Chem Industries, Mumbai (State- Maharashtra, India), PVP K30, Talc and Titanium Dioxide were obtained from Thermosil Fine Chem Industries, Pune (State- Maharashtra, India).

College of Pharmacy provided all the Excipients, Akkalkuwa and all the chemicals used were of Analytical Grade.

Extraction of Bee Propolis: The raw Bee propolis were washed with distilled water to clean the surface and then were extracted with 70 % ethanol [1] in a 40:50 ratio, then, the extract was filtered and further dried in an oven at 45°C (not exceeding 50 ^{0}C). Then pass the dry extract powder through an 80# mesh sieve and calculate the % yield.

Design of Factorial Batches: All the batches, *i.e.*, F1-F9, were designed with the help of design expert software.

TABLE 1: FACTORIAL DESIGNED BATCHES

Ingredients (mg/tablet)	F1	F2	F3	F4	F5	F6	F7	F8	F9
Ibuprofen	200	200	200	200	200	200	200	200	200
Bee Propolis	40	40	40	65	65	65	90	90	90
Hpmc K200m	20	40	60	20	40	60	20	40	60
Lactose	97	77	57	72	52	32	47	27	7
Pvp K30	26	26	26	26	26	26	26	26	26
Talc	7	7	7	7	7	7	7	7	7
Magnesium Stearate	10	10	10	10	10	10	10	10	10
Titanium Dioxide	Q. S.	Q. S.	Q. S.	Q. S.	Q. S.	Q. S.	Q. S.	Q. S.	Q.S.
Total Weight	400	400	400	400	400	400	400	400	400

Preparation of Granules: The granules of the formulation were made by the wet granulation technique; water was used as a granulating agent, and after granulation, the granules were passed through a 60# mesh sieve.

Compression of Granules: The compression of granules was performed on a 9- stationed tablet compression machine [Rimek model: DL 09 Stationed Tablet Compression Machine, Karnavati Engineering, (Mehsana, Gujarat, India) equipped with 9 mm of Round shaped punches and further studied for post-compression parameters.

RESULTS AND DISCUSSION:

A. Determination of Melting Point: The melting point of Ibuprofen API was determined by the capillary tube method. The Melting point was found within the standard range of 75-77°C.

B. Calibration curve of Ibuprofen (Pure Drug):

Calibration curve of Ibuprofen in 0.1 N HCL: A standard curve was prepared by dissolving 100 mg of Ibuprofen in 100 ml of 0.1 N HCL and further diluted to 0.1 N HCL to get the solution in the concentration range of 0-10 µg/ml. The absorbance values were determined at 222 nm.

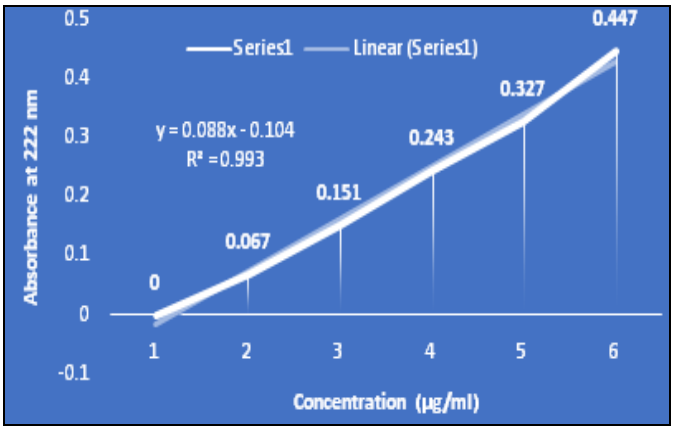

FIG. 1: STANDARD CALIBRATION CURVE OF IBUPROFEN IN 0.1 N HCL

TABLE 2: STANDARD CALIBRATION CURVE OF IBUPROFEN IN 0.1 N HCL

Concentration (µg/ml)	Absorbance (Mean ± SD)
0	0
2	0.067
4	0.080
6	0.243
8	0.327
10	0.356

Calibration curve of Ibuprofen in 7.4 pH Phosphate Buffer: A standard curve was prepared by dissolving 100 mg of Ibuprofen in Phosphate Buffer pH 7.4 and make up to a volume of 100 ml. it was further diluted to get the solution in the concentration range of 0-10 µg/ml. The absorbance values were determined at 222 nm.

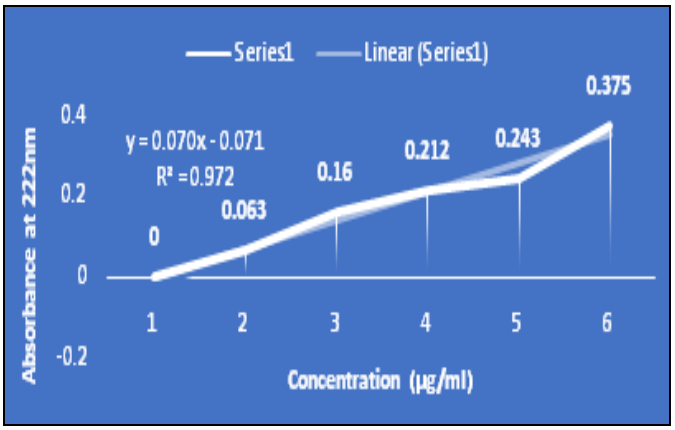

FIG. 2: STANDARD CALIBRATION CURVE OF IBUPROFEN IN 7.4 pH PHOSPHATE BUFFER

TABLE 3: STANDARD CALIBRATION CURVE OF IBUPROFEN IN 7.4 pH PHOSPHATE BUFFER

Concentration (µg/ml)	Absorbance (Mean ± SD)
0	0
2	0.063
4	0.160
6	0.212
8	0.243
10	0.375

C. FTIR Studies:

FTIR of Ibuprofen (Pure Drug):

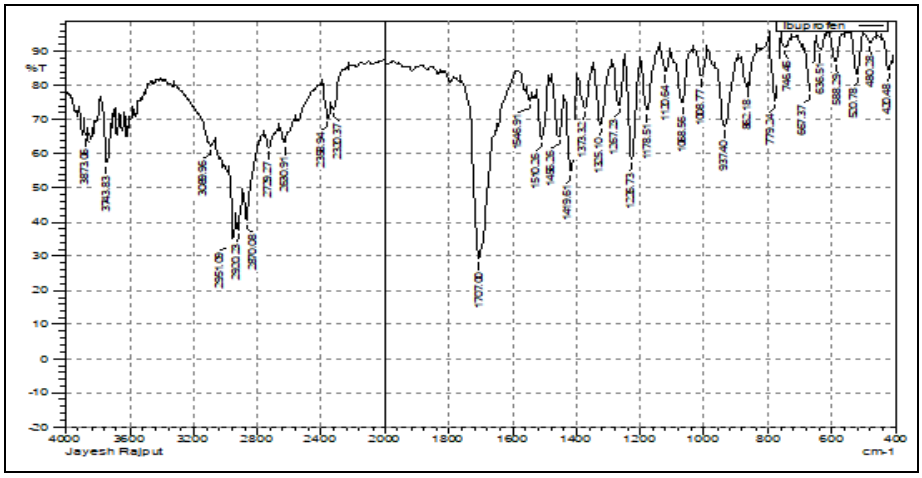

FIG. 3: - FTIR OF IBUPROFEN (PURE DRUG)

TABLE 4: INTERPRETATION OF FTIR OF IBUPROFEN (PURE DRUG)

Functional Group	Characteristics Peaks Cm^{-1}
C-H Stretching	3089.96
O-H Stretching	2951.09
Aromatic Out-Plane Bending C-H	937.40
C=O Stretching	1707.00

FTIR Spectra of "Bee Propolis" (Natural Polymer):

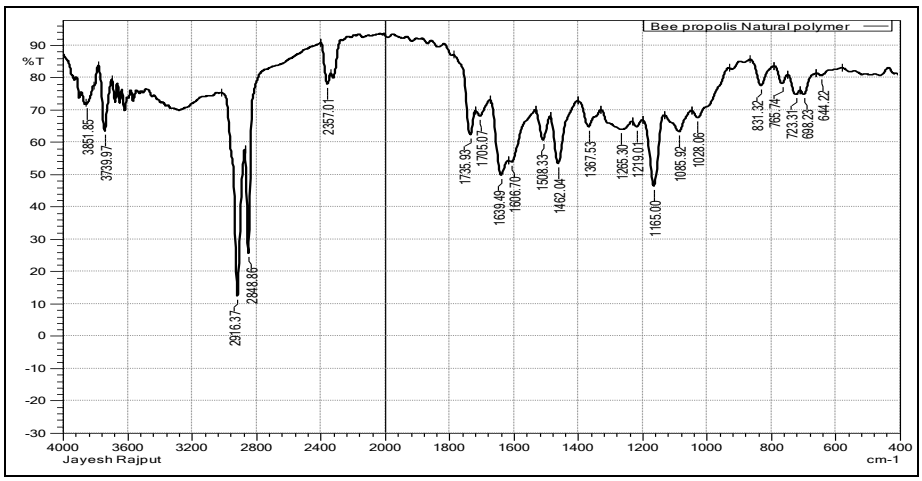

FIG. 4: FTIR OF "BEE PROPOLIS" (NATURAL POLYMER)

FTIR Spectra of HPMC K200 M (Synthetic Polymer):

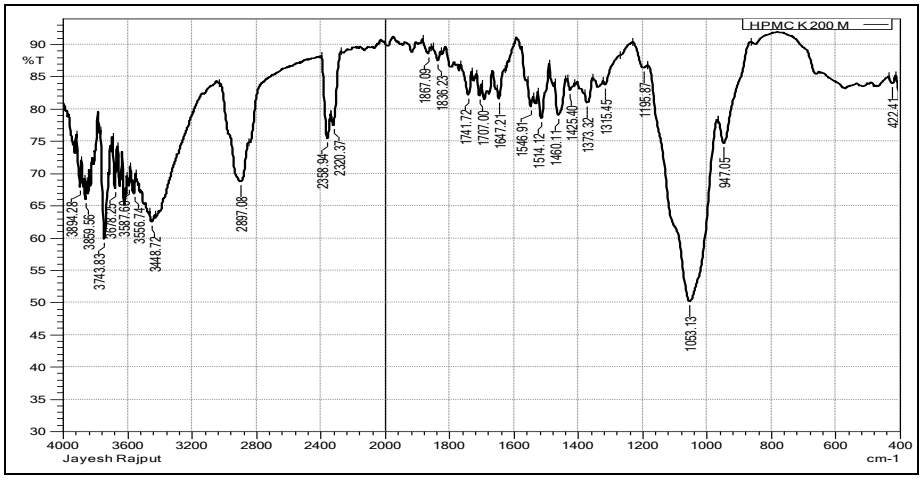

FIG. 5: FTIR OF HPMC K200 M (SYNTHETIC POLYMER)

FTIR Spectra of Blend of Factorially Designed Batches:

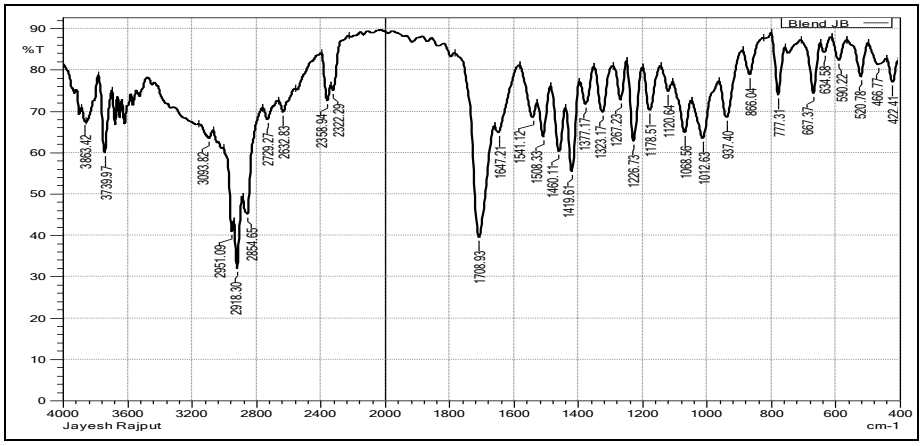

FIG. 6: FTIR OF BLEND OF FACTORIALLY DESIGNED BATCHES

D. DSC Studies:

DSC graph of Ibuprofen (Pure Drug):

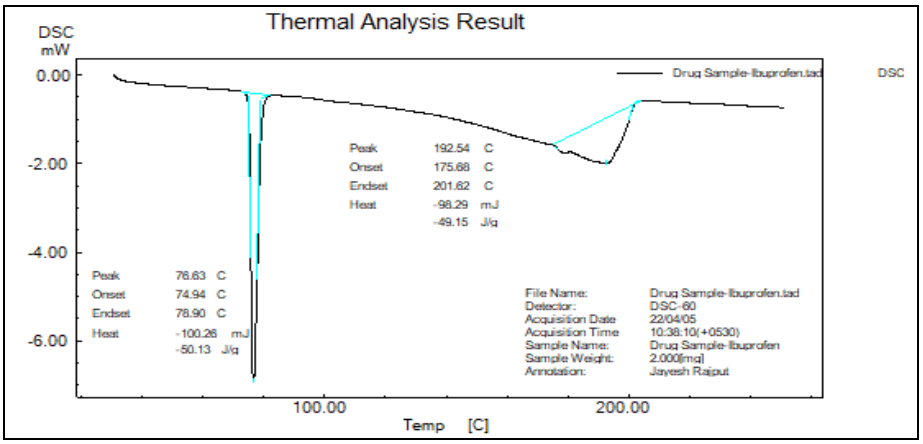

FIG. 7: DSC GRAPH OF IBUPROFEN (PURE DRUG)

DSC graph of Blend of Factorially Designed Batches:

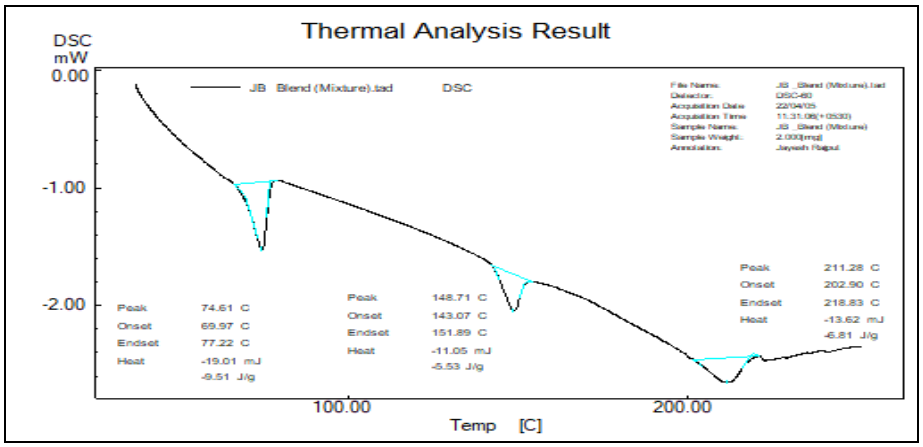

FIG. 8: DSC GRAPH OF BLEND OF FACTORIALLY DESIGNED BATCHES

E) Evaluation of Sustained Release Matrix Tablet:

i. **Appearance:** The tablets were observed visually and did not show any defects, such as Overlapping, chipping, and Lamination.

ii. **Dimensions (Thickness and Hardness):** The size/diameter of the tablets of all formulations was 5.124 ± 0.05 to 5.296 ± 0.02 nm.

iii. Tablet Hardness: The hardness of tablets was measured by a Monsanto hardness tester, and the hardness of tablets was found to be in the range of 5.22 ± 0.06 kg/cm^{2}to 6.90 ± 0.02 kg/cm^2. This indicates good tablet strength.

iv. Friability Test: Friability test was done in Friability Apparatus [Electrolabs, Ltd, EF2 (USP) (Type-II Apparatus)]. The friability test or percent friability of all the formulations was found between 0.304 ± 0.08 % to 0.755 ± 0.02 %. This indicates the good handling property of the prepared sustained release tablet.

v. *In-vitro* Drug Release Study of Optimized Batches: The *in-vitro* dissolution studies of the factorially designed tablet batches were studied for 10 h, first two hours *i.e.*, 0-2 hrs in 0.1 N HCL and the rest i.e., 3-10 hrs in pH 7.4 Phosphate Buffer and the results obtained were given in the table and figure given below.

TABLE 5: *IN-VITRO* DRUG RELEASE (0-10 HR) OF OPTIMIZED FORMULATION (F1-F9)

Time (Hrs)	Cumulative % Drug Release (% CDR)								
	F1	F2	F3	F4	F5	F6	F7	F8	F9
0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
1	12.63	12.62	12.75	12.47	12.69	12.92	12.78	12.65	12.66
2	12.83	12.66	12.81	12.49	13.15	12.93	12.80	12.67	12.88
3	15.73	14.22	15.39	12.66	17.39	14.41	15.74	15.48	15.71
4	22.12	19.65	22.40	16.42	24.61	24.18	24.05	24.06	22.99
5	28.47	24.42	29.61	24.75	26.77	28.15	28.01	28.66	28.27
6	32.32	28.44	36.58	32.01	37.98	32.06	30.36	29.71	31.12
7	44.44	37.51	47.93	50.49	46.32	39.69	42.48	44.76	43.87
8	68.63	63.54	70.77	72.86	67.02	64.07	63.97	61.73	63.09
9	82.41	78.01	85.01	76.63	80.65	77.24	77.45	79.76	78.18
10	95.32	93.42	96.57	94.65	93.17	94.34	92.44	91.82	93.38

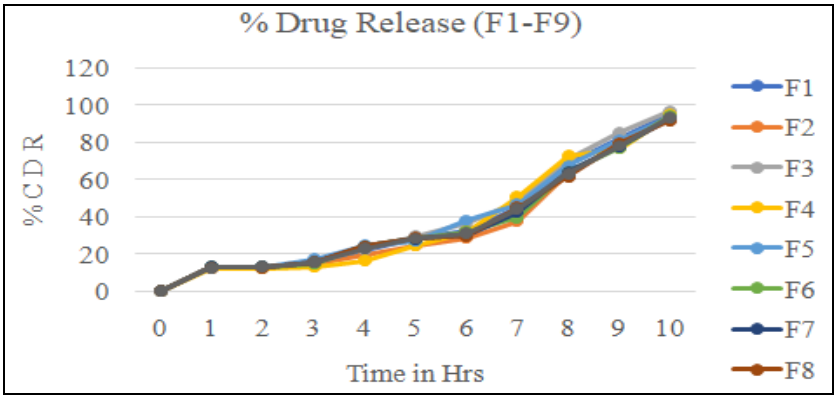

FIG. 9: *IN-VITRO* DRUG RELEASE (0-10 HR) OF OPTIMIZED FORMULATION (F1-F9)

The release of all formulations was companied and evaluated. The results showed that the formulations give more drug release were considered optimized and further studied for stability studies.

Stability Studies: Stability Study is carried out on formulation batch (F3) according to ICH guidelines. The tablet did not show any physical changes during the study period. The drug content was found to be 98.56 ± 1.44 % for Ibuprofen at the end of 1 month on stability conditions shown in the table below.

TABLE 6: STABILITY STUDY OF OPTIMIZED BATCH (F3)

Temperature	Time in Months	Hardness (kg/cm^2)	Friability (%)	Drug Content (%)	% Drug Release
40° C ±2°C 75% RH± 5% RH	0	5.22 ± 0.06	0.731 ± 0.02	99.77 ± 1.23	96.57 %
40°C ±2°C 75% RH± 5% RH	1	5.13 ± 0.10	0.651 ± 0.05	98.56 ± 1.44	93.56 %

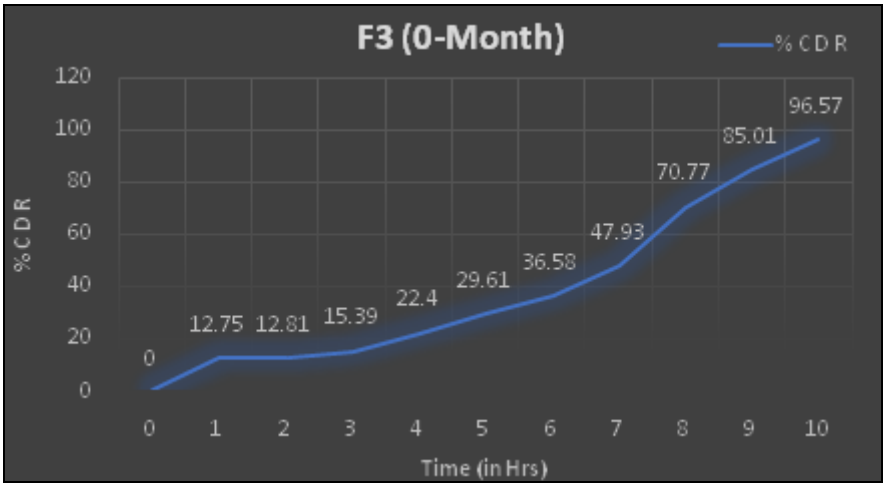

FIG. 10: DISSOLUTION PROFILE OF OPTIMIZED BATCH (F3) AFTER 0 MONTH UNDER STABILITY PERIOD

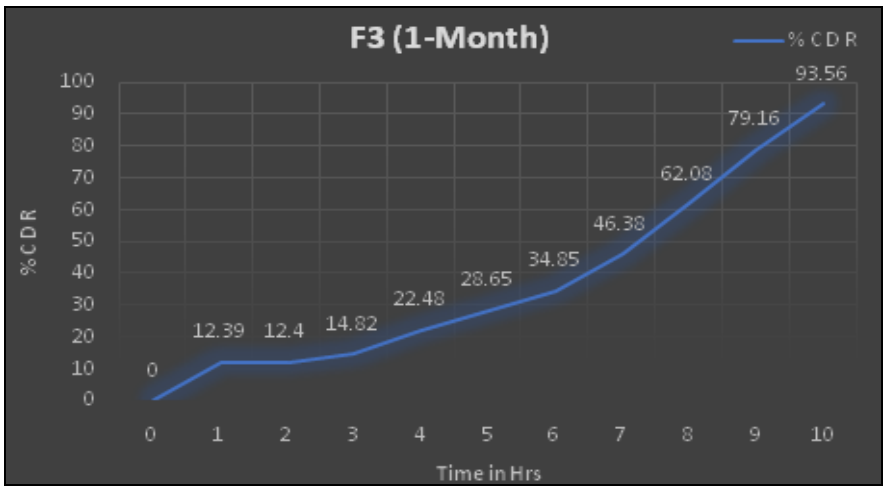

FIG. 11: DISSOLUTION PROFILE OF OPTIMIZED BATCH (F3) AFTER 1 MONTH UNDER STABILITY PERIOD

CONCLUSION: Aim of the study was to formulate, optimize and evaluate matrix tablets of Ibuprofen. Ibuprofen matrix tablets were formulated by using the active pharmaceutical ingredient (drug), the Bee Propolis (Natural Polymer), and HPMC K200 M (Synthetic Polymer). The Bee Propolis and HPMC K200 M with their proportions, it can be seen that by increasing the concentration of Bee Propolis and decreasing the concentration of HPMC K 200 M in the formulation, the drug release rate from the tablets was found to be increased in formulation number F3, using this ratio of drug and polymer, gives optimum release, **i.e.,** Drug; Bee Propolis; HPMC K200 M; PVP K30; Talc; Magnesium Stearate; Lactose.

In this F3 showed satisfactory results. But when the concentration of HPMC K200 M increased and Bee Propolis decreased, the drug release rate was found to be 96.57 %, from the formulations F1-F9, the formulation F3 was selected as an optimized formulation because it showed maximum drug release, *i.e.*, 96.57 % in 10 Hrs and the compatibility of Ibuprofen with polymers HPMC K200 M and Bee Propolis. The studies of FTIR show that all of the above characteristic peaks of Ibuprofen were observed near their respective values. So, it has been concluded that there is no incompatibility between polymers and pure drugs. The preliminary examination of Ibuprofen, like its melting point, obtained in range from 75-77°C by capillary tube method using Thiele's Tube and liquid paraffin to check the melting point. Calibration curves were taken in 0.1 N HCL pH 1.2 and 7.4 pH Phosphate Buffer at 222 nm by using UV Spectrophotometer (Dual Beam).

The physical study of formulation like its hardness, friability, thickness, weight variation, surface pH, drug content uniformity, *in-vitro* residence time, *etc*. have been performed. The hardness was found

in the range of 5.22 ± 0.06 kg/cm^2 and 6.90 ± 0.02 kg/cm^2. The hardness result shows that as increase in polymer concentration will increase the hardness of tablets. The percentage friability was good in the range of 0.304 ± 0.08 % to 0.755 ± 0.02 %, and the normal range of friability is below 1 % by the standards of Indian Pharmacopoeia (IP).

The thickness is ranged in 5.124 ± 0.05 to 5.296 ± 0.02 mm. The weight variation of all trial and factorial designed formulation batches was found between 397.95 ± 2.05 to 399.25 ± 0.75 mg. The obtained results indicate that all the tablets of different formulations were within the IP specifications. The average of drug content was found in between the range of 98.54 ± 2.46 to 99.98 ± 1.02 %. The *In-vitro* drug dissolution studies were carried out for 0-10 Hrs on formulation F1-F9, and the percentage of drug release was found to be in the range of 91.82% to 96.57%; the stability study was performed according to ICH guidelines, and the tablet showed very minute or little changes on its physical appearance like hardness.

The percentage of drug release of tablets kept in two different stability conditions (40°C ± 2°C, 75% RH) for 0- and 1-month periods were found to be 96.57% and 93.56%. All the results are found within the pharmacopeial limit; it passes all of the tests. By adding Bee Propolis to the Ibuprofen API and making a matrix tablet will give a synergistic approach towards Analgesic, Antipyretic and Anti-inflammatory activities of the formulation; in a research paper by Katarzyna Grecka and Piotr Szweda [1], they concluded that "by the broth, microdilution checkerboard assay revealed synergistic interactions between all investigated antipyretics namely acetylsalicylic acid, Ibuprofen and Acetaminophen with ethanolic extracts of propolis on the growth of Staphylococcus Aureus" means synergism for antibacterial and antipyretic effect.

In another research article by Liping Sun, *et. al.,* [2], the author combined Ibuprofen with Chinese bee propolis and tested *in-vivo* by Acetic Acid Writhing Test, Tail-immersion Test, and Hot Plate Test authors concluded that while combining bee propolis with Ibuprofen it gives the synergistic effects for Antinociceptive (compounds capable of diminishing pain without negative effects on consciousness or without producing anaesthesia) and pain-relieving therapeutic activities. In this work, only physicochemical characterization, formulation development, and *in-vitro* evaluation of matrix tablets of Ibuprofen were done, along with *in-vitro* release study *in-vivo* release behaviour of the drug is also important. So, future in-vivo release studies using different models are required to set the in-vitro, in-vivo correlation necessary for the development of successful formulation, and long-termstability studies are necessary for the further future prospects.

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CONFLICTS OF INTEREST: The author declares no conflict of interest.

REFERENCES:

1. Katarzyna Grecka and Piotr Szweda: Synergistic Effects of Propolis Combined with 2-Phenoxyethanol and Antipyretics on the Growth of Staphylococcus aureus. Pharmaceutics 2021; 13: 215. https://doi.org/ 10.3390/pharmaceutics13020215. Pg. 1-17.
2. Liping Sun, Lei Liao and Bei Wang: Potential Antinociceptive Effects of Chinese Propolis and Identification on Its Active Compounds. Hindawi Journal of Immunology Research Volume Article ID 5429543, 6 pages https://doi.org/10.1155/2018/5429543.
3. Katekhaye S, Fearnley H, Fearnley J, Paradkar and Anant R: Gaps in Propolis Research: Challenges Posed to Commercialisation and the Need for an Holistic Approach. Journal of Apicultural Research 2019; 58(4): 604-616. https:// doi.org/10.1080/00218839.2019.1614273. pg. 1-37.
4. Deepak M. Kasote: Propolis: A Neglected Product of Value in the Indian Beekeeping Sector. Bee World 2017; 94(3): 80-83, DOI: 10.1080/0005772X.2017.1345223. pg. 80-83.
5. Houghton PJ: Propolis as a medicine. Are there scientific reasons for its reputation? In: Munn P, editor. Beeswax and Propolis for pleasure and profit. Cardiff, UK: International Bee Research Association 1998; 10.
6. Boryana Trusheva, Dorina Trunkova and Vassya Bankova: Different extraction methods of biologically active

components from propolis. A Preliminary Study 2007; 1-4. doi:10.1186/1752-153X-1-13. Pg.

7. Supakit Khacha-ananda, Khajornsak Tragoolpua, Panuwan Chantawannakul and Yingmanee Tragoolpua: Antioxidant and anti-cancer cell proliferation activity of propolis extracts from two extraction methods. Asian Pac J Cancer Prev 2013; 14(11): 6991-6995.
8. Jasvir Singh Dalio: Factors effecting propolis collection behaviour of *Apis mellifera* L. International Journal of Current Innovation Research 2018; 4(3): 1092-1094.
9. Edna D‟ Souza, Jyoti Mantri and Arjumanara Surti: Primary screening of multipotent therapeutic properties exhibited by Indian propolis. Indian Journal of Natural products and Resources 2016; 7(2): 135-140.
10. Prem Jose Vazhacharickal: A review on health benefits and biological action of honey, propolis and royal jelly. Journal of Medicinal Plants Studies 2021; 9(5): 01-13.
11. Ghisalberti EL: Propolis: A Review. Bee World, 1979; 60: 2, 59-84, DOI: 10.1080/0005772X.1979.11097738.
12. Izabela Przybyłek and Tomasz M: Karpi ´nski Antibacterial Properties of Propolis. Molecules 2019; 24: 2047; doi:10.3390/molecules24112047. Pg. 1-17.
13. Kai Liang Yeo, Choe Peng Leo1 and Derek Juinn Chieh Chan: ultrasonic enhancement on propolis extraction at varied ph and alcohol content 2014; 1-9.
14. Propolis: the beehive‟s immunitary system. www.bnatural.it. scientifically-based concepts and ideas for formulating products with M.E.D. Propolis.
15. Laerte M. Santos, Maísa Santos da Fonseca, Ana Rita Sokolonski, Kathleen R. Deegan, Roberto PC. Araújo, Marcelo A. UmszaGuez, Josiane D. V. Barbosa, Ricardo D. Portela and Bruna AS: Machado. Propolis: Types, composition, biological activities and veterinary product patent prospecting. Journal of the Science of Food and Agriculture 100(4): 1369- 1382.
16. Bernd König: Plant Sources of Propolis, Bee World, 1985; 66: 4, 136-139, DOI: 10.1080/0005772X.1985.11098844.
17. Andresa Aparecida Berretta, Marcelo Augusto Duarte Silveira, Jos´e Manuel Condor´ Capcha and David De Jong: Propolis and its potential against SARSCoV-2 infection mechanisms and COVID19 disease Running title: Propolis against SARS-CoV-2 infection and COVID-19. Research. https://doi.org/10.1016/j.biopha.2020.110622. Pg. 1-16.
18. Ary Fernandes Júnior, Elaine Cristina Balestrin, Joyce Elaine Cristina Betoni, Ricardo de Oliveira Orsi, Maria de Lourdes Ribeiro de Souza da Cunha and Augusto Cezar Montelli: Propolis: antiStaphylococcus aureus activity and synergism with antimicrobial drugs. Mem Inst Oswaldo Cruz, Rio de Janeiro 2005; 100(5): 563-566.
19. Wawat Rodiahwati, Ariskanopitasari and Imam K Saleh: Identification of total bioflavonoid compound of propolis extract from wild honey bee hive apis dorsata in sumbawa region. Indonesia Applied science and Engineering Progress 2019; 12(1): 37-43, 2019. DOI: 10.14416/j.ijast.2019.01.007.
20. Ayşegül Aylin Aytekin, Sakine Tuncay Tanrıverdi, Fadime Aydın Köse, Didem Kart, İpek Eroğlu & Özgen Özer: Propolis Loaded Liposomes: Evaluation of Antimicrobial and Antioxidant Activities, Journal of Liposome Research, DOI: 10.1080/08982104.2019.1599012.
21. Wendy Leticia Guerra-Ponce, Sandra Leticia Garcia-Vásquez, Patricia González-Barranco, Ivonne Antonieta Camacho-Mora, Yolanda Araceli Garcia-Vásquez, Elizabeth Orozco-Beltrán and Linda Anne Felton: *In-vitro* evaluation of sustained released matrix tablets containing ibuprofen: a model poorly water-soluble drug. Brazilian Journal of Pharmaceutical Sciences vol. 52, n. 4, oct./dec., 2016 http://dx.doi.org/10.1590/S1984-82502016000400020. Pg. 751-759.
22. Carla M. Lopes, José Manuel Sousa Lobo, Paulo Costa and João F. Pinto: Directly Compressed Mini Matrix Tablets Containing Ibuprofen: Preparation and Evaluation of Sustained Release. Drug Development and Industrial Pharmacy 2006; 32: 95–106. DOI: 10.1080/03639040500388482.

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