FORMULATION AND EVALUATION OF PH-DEPENDENT SUSTAINED RELEASE TABLET OF BEMPEDOIC ACID

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ABSTRACT
The main goal about this research had been to create a sustained release tablet formulation that is pH-dependent for Bempedoic Acid, a drug that is acid labile and poorly soluble in water in the stomach environment. The objective of formulation is to enable the dose form that the stomach will not dissolve, it begins break down in upper small intestine, as well as to release the active ingredient gradually and under controlled circumstances. As part of the preformulation investigations, the drug-excipient compatibility, and partition coefficient were examined. In order to create a sustained release tablet that is pH-dependent, Eudragit® L100 and Eudragit® S100 were combined. It was established how the drug release rate was affected by the solubilizer, binder, coated concentration of polymers, plasticizer, and pore former. The findings showed that while no drug was found when the drug was submitted to release of drugs experiments in hydrochloric acid at 0.1 mol/L for two hours, almost within 12 hours, 90% of the medication was released in the pH 6.8 phosphate buffer in a sustained release fashion. The coated film's pore development and/or stress sites were engaged in the drug release mechanism. For three months, the coated tablets remained stable at 40°C with a relative humidity of 75%. These outcomes demonstrated a viability in the coated tablet system containing Bempedoic Acid, which could aid in the effective management of cardiovascular illness.

INTRODUCTION:

The word "dyslipidaemia's" describes conditions that cause abnormal levels of circulating lipids to occur or present as such. The invention's compositions are given to a sufferer in order for bring their blood lipid levels back to normal, if they are abnormally high[1]. Medical treatises well-known to experts in the field report normal amounts of lipids. For instance, the American Heart Association and the National Heart, Lung, and Blood Institute's National Cholesterol Education Program both have websites with suggested amounts of free triglycerides, hdl, ldl, and other having to do with lipid metabolism. It is advised that blood have an hdl cholesterol level of above 35 milligrams/dL and a less than 130 mg/dL of ldl cholesterol. The optimal ratio of ldl versus hdl lipids in blood is 3.5:1, and the blood's suggested number of free triglycerides is less than 200 mg/dL[2].

Heart and circulatory system disorders are referred to as "cardiovascular diseases. "Frequently, dyslipoproteinemias and/or dyslipidaemias are linked to these illnesses. Atherosclerosis, ischemia, stroke, endothelial dysfunctions, and arteriosclerosis, particularly the compositions of the present invention are suitable for the prevention or treatment of cardiovascular disorders, including those that influence blood vessel elasticity, peripheral vascular disease, coronary heart disease, myocardial infarction, cerebral infarction, and restenosis. Generally speaking, "sustained release" describes a dosage form that is intended to release a medication at a predefined rate, which need not be constant, to maintain a desired range of drug concentration over a given amount of time, such as eight hours, twelve hours, sixteen hours, twenty hours, twenty-four hours, etc., with the least amount of side effects possible[3]. As demonstrated by the bempedoic acid sustained release formulations discussed above, this can be accomplished using a range of formulations. Drugs are almost often delivered as prepared getting ready to medications (dosage forms or drug delivery systems) rather than as pure chemical molecules alone[4]. By using the proper excipients or additives in the formulations, they can range from quite straightforward solutions to intricate drug delivery systems[5]. In order to provide a variety of acceptable preparations or dosage forms, formulation additives change the dissolution, become harder, retain, maintain, and emulsified, increase compression pharmacological chemicals. Numerous elements need for be taken into account before a pharmacological substance may be effectively formed into a dosage form. These fall into the following three categories in general[6].

1) Biopharmaceutical variables, such as elements influencing how well a medicine is absorbed through various modes of administration.

2) Drug-related aspects, such as the substance's chemical and physical characteristics[7]

3) Therapeutic variables, such as taking the clinical indication into account only when every variable is taken into account and connected to the others will effective and high-quality medications be created and made. This is the fundamental idea behind the design of dosage form. When giving medications for systemic effects, using oral method is preferred crucial path of delivery[8-9]. Any medication administration system's objective is to provide an effective dosage for the medicine with appropriate where abouts or sites allows the human body can easily arrive in order to subsequently maintain a target medication concentration[10]. This site at which a drug has delivered drug via the system should be determined by the patient's factors and the body requirements over a predetermined treatment time[11].

Sustained drug release dosage forms are a recent development that gives a longer-lasting medicinal effects, improved drug administration management, and fewer side effects[11-12.] Sustained release dosage forms often aim to sustain therapeutic medication levels within blood from or tissue over an extended amount time in general. Usually, this is done to get the release in zero-order[13]. Typical pharmacological kinetics dose formulations with instantaneous release, regulated a zero-order delivery as well as continuous release[14]. The medication level in relation to time profile[15]. The dosage forms for quick release (up from a

traditional granule and a capsule), prolonged release (a first-order slowly),[16] or zero order discharge (controlled release). When a medicine is supplied by a typical drug delivery method, its blood concentration first increases, peaks, and then nearly drops[17-18]. There is a minimum effective concentration and a maximum safe concentration for every medicine[19].

MATERIAL AND METHOD:

MSN Laboratories, Hyderabad, has provided a complimentary sample of Bempedoic acid, we purchase Eudragit L, Eudragit S Diethyl Phthalate, Propylene Glycol, Magnesium Stearate, Talc, Povidone K30 from Modern Industries in Nashik. The remaining reagents were all analytical grade and were acquired from Thermofisher Scientific India Pvt. Ltd.

Wet granulation method for tablet formulation

Tablets were made using the traditional wet granulation technique[20]. All ingredients were well combined and put through sieve number 60, with the exception of glidants and lubricant. Granulation was carried out using a solution of povidone K 30 and enough water in a predetermined amount[21]. After going through filter number 12, the wet matter was dried for two hours at 50 °C[22-23]. Using a single station tablet punch machine, the dry granules were compacted into tablets after being lubricated with talc and magnesium stearate[24-25]. Then applying Eudragit Land coating material on the tablet Using plasticizer propylene glycol and pore forming diethyl phthalate, Eudragit S was applied to the coating pan[26].

Table 1. Trial Batches of formulation of Bempedoic Acid

Components	F1	F2	F3	F4	F5	F6	F7	F8
Bempedoic Acid(mg)	180	180	180	180	180	180	180	180
Eudragit L: Eudragit S	1:2	1:4	1:2	1:4	1:2	1:4	1:2	1:4
Sodium Dodecyl Sulphate	10	15	10	15	10	15	10	15
Ethanol	5	5	5	5	5	5	5	5
Povidone K30	20	25	20	25	20	25	20	25
Polyethylene Glycol(mg)	1	1	1	1	1	1	1	1
Diethyl Phthalate	1	1	1	1	1	1	1	1
Lactose	10	15	10	15	10	15	10	15

RESULT AND DISCUSSION:

Melting Point

The melting point of Bempedoic acid was determined using the capillary method. The melting point was found to be in range between 87°C and 92°C, which is identical to the reported melting point**.**

Study on Bempedoic Acid saturated solubility in distilled water

The Saturated solubility of Bempedoic acid was determined in distilled water and found to be 0.168µg/mL. According to the BCS classification system the solubility of drug in water is below the significant solubility value and hence the drug is said to be poorly water soluble.

FTIR of Bempedoic Acid

Table 2. Functional group and IR ranges of Bempedoic Acid

Sr.No.	Functional Group	IR ranges
1	O-H Stretching	3441cm^{-1}
2	C=O Stretching	2939cm^{-1}
3	C-H Stretching	1114cm^{-1}
4	RCOO Stretching	1712cm^{-1}

Differential Scanning Calorimetry

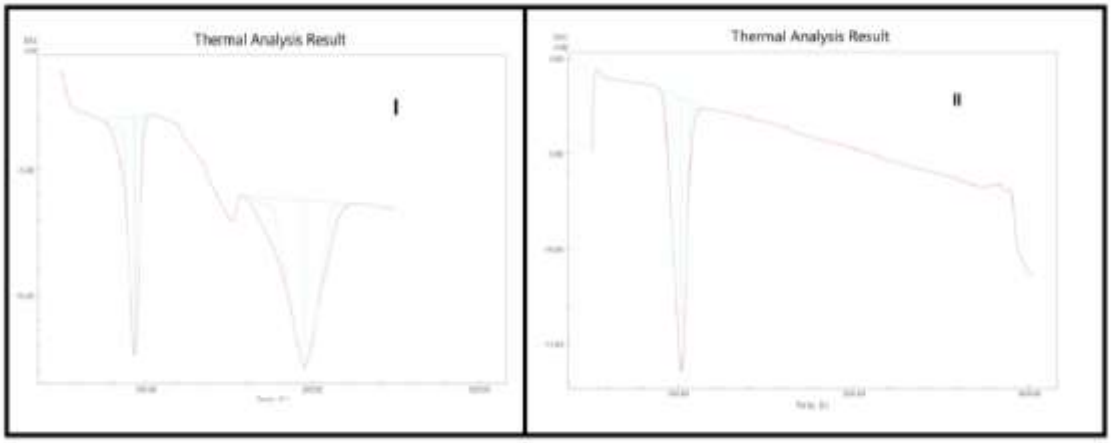

Figure 1: I -DSC thermogram of Physical Mixture of Drug and Polymer and II -DSC of Bempedoic Acid

To verify the compatibility of the substances, For the DSC examination, DSC thermograms were acquired for the endothermic reaction of Eudragit L:Eudragit S and pure Bempedoic Acid using a DSC-60 equipment (M/s Shimadzu).

Pre-compression Characteristics

Table 3. Pre-compression characteristics of powder mixture

Formulas	Bulk density(g/cm^3)	Tapped density(g/cm^3)	Angle of repose(Ɵ)	Hausner's ratio	Carr's index (%)
F_1	0.51±0.24	0.55±0.12	29.12±0.20	1.07±0.12	4±0.26
F_2	0.48±0.21	0.53±0.11	21.15±0.3	1.10±0.03	5±0.23
F_3	0.49±0.20	0.69±0.12	24.12±0.14	1.40±0.01	20±0.12
F_4	0.50±0.23	0.62±0.14	25.82±0.19	1.24±0.02	12±0.26
F_5	0.49±0.20	0.72±0.14	24.11±0.17	1.46±0.04	23±0.25
F_6	0.55±0.01	0.73±0.25	28.17±0.27	1.32±0.02	18.00±0.25
F_7	0.50±0.15	0.57±0.03	27.85±0.17	1.14±0.01	7.04±0.24
F_8	0.49±0.11	0.500±0.1	23.36±0.7	1.02±0.02	1.11±0.28

Tablet Evaluation

Thickness: The optimized formulations' average thickness was determined to be between 3 and 4 mm, falling within the permitted deviation range of ± 5% of the standard value.

Friability: The % friability of each sustain release tablet formulation was assessed. The improved formulations' average percentage friability was determined to be under the pharmacopeial limit, specifically within 0.6134%, or less than 1%.

Weight Variation: An electronic balance is used to determine the average weight of twenty tablets. Every tablet's weight is determined individually and contrasted with the average weight. If there are no more than two tablets that deviate from the % restriction and if there are no tablets that differ by more than twice the percentage limit, the tablets meet USP requirements.

Hardness: A hardness test was conducted by "Monsanto hardness tester". Optimized formulation possesses a hardness that ranges from 3.5 to 5 kg/cm2. This guarantees that every formulation batch has favourable handling qualities.

Table 4. Post Compression Evaluation of tablet

Formulas	Hardness (kg/cm^2)±SD	Friability (%) ±SD	Thickness (mm)±SD	Weight variation (mg)±SD
F_1	3.9±0.08	0.90±0.10	3.11±0.01	315.61±0.07
F_2	4.8±0.05	0.81±0.11	3.05±0.15	319.1±0.06
F_3	3.5±0.03	0.70±0.13	2.75±0.12	310.33±0.03
F_4	4.8±0.8	0.63±0.12	2.92±0.21	318.41±0.06
F_5	3.9±0.1	0.71±0.14	2.87±0.12	320.12±0.04
F_6	3.5±0.09	0.86±0.23	3.55±0.27	317.02±0.04
F_7	3.7±0.15	0.67±0.03	2.87±0.19	318.02±0.03
F_8	4.5±0.15	0.79±0.1	2.55±0.3	320.45±0.01

Dissolution Analysis: The type-II USP apparatus used to study dissolution rate in pH of 900 ml of phosphate buffer (6.8) at 50 rpm, maintaining 37 degrees Celsius ±5°C. The filtered solution was taken out and filtered every 10 minutes, and the medication concentration was established utilizing the ultraviolet (UV) spectrophotometric method that 209 nm.

Table 5. In-vitro Drug Release

Time	F1	F2	F3	F4	F5	F6	F7	F8
0	0.68	1.11	1.89	2.11	11.23	3.04	3.73	4.61
1	2.87	3.09	4.86	10.91	19.35	6.21	5.68	7.12
2	6.41	7.35	9.89	16.31	27.91	9.54	7.32	10.93
3	11.54	10.05	15.32	21.08	34.85	13.67	12.63	17.35
4	19.58	17.25	21.74	30.71	39.05	22.45	23.65	25.72
5	26.36	25.36	28.02	39.87	48.76	34.91	31.74	34.56
6	33.41	36.75	38.14	46.96	56.77	41.76	40.13	43.22
7	42.07	43.42	45.04	54.17	65.66	49.63	48.48	50.72
8	51.46	62.69	64.94	65.49	74.26	58.48	57.18	61.03
9	60.75	73.31	71.42	74.28	83.69	69.34	68.57	70.57
10	75.03	81.48	82.48	86.19	91.26	78.24	77.26	79.17
11	84.65	89.78	90.52	91.91	95.17	88.35	86.45	94.73
12	90.2	92.38	94.01	95.85	97.73	93.78	92.82	96.73

Percentage Drug Release:

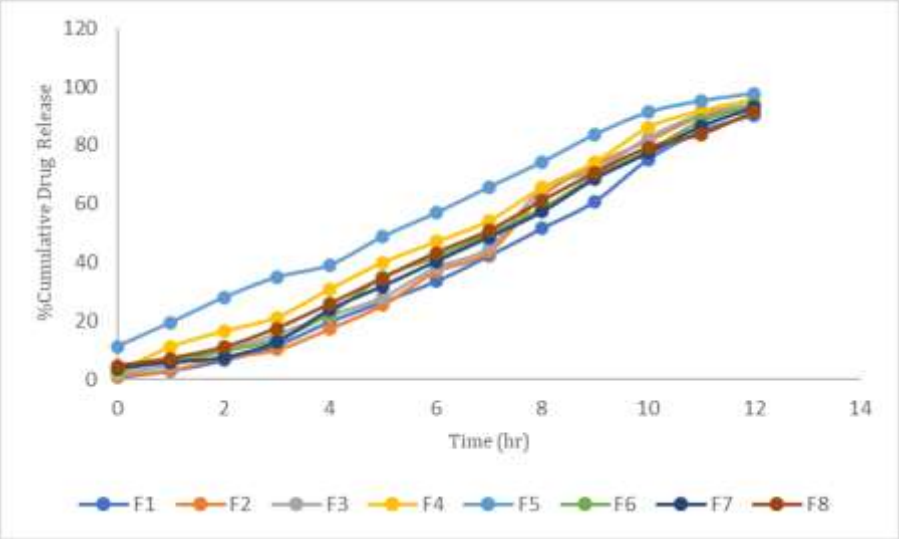

Figure 2: Percentage of Cumulative Drug Release

Conclusion

In F8 Batch, it was discovered that the pre-formulation investigations, which included the Carr's index, Hausner's ratio, bulk density, and tapped density, and angle for repose of formulations, were everyone within an accepted bound. Following compression, the powder mixtures were assessed to post-compress characteristics like drug content, hardness, size variation, and Friability testing. Results from the F8 formulation batch were satisfactory. Using a USP Type-II dissolving device the medication release in vitro was examined at pH 6.8 Phosphate buffered. Results showed that formulations F8 (96.73%) at 12 hr to create a sustained release tablet formulation that is pH-dependent. for bempedoic acid, a model medication, which is acid labile and inadequately soluble in water in the stomach microenvironment. The goal is the formulation was to pass through the stomach, get started release in the small intestine, additionally to discharge the dynamic ingredient slowly and in controlled manner. Preformulation research focused at drug-excipient compatibility, partition coefficient. Eudragit® L100 and Eudragit® S100 have been combined to create a pH-dependent long-term release tablet. The drug release rate, an effect of pore former, plasticizer, disintegrant, binder, covered polymer concentration, and solubilizer were examine.

CONFLICT OF INTEREST: The authors have no conflicts of interest regarding this investigation.

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REFERENCES

1. Patil AS, Joshi SS. Formulation and evaluation of verapamil hydrochloride sustain release tablet. Research Journal of Pharmacy and Technology. 2024;17(2): 802-6.DOI- 10.52711/0974-360X.2024.00124
2. Shinde AJ, Khandekar SS, Bhatia MS, Tamboli FA, Jarag RJ, More HN. Comparative evaluation of formulations designed using chemically modified pectin and eudragit for sustained release of nateglinide. Research Journal of Pharmacy and Technology. 2023;16(12): 5775-81.DOI-10.52711/0974-360X.2023.00935
3. Parija S, Mohanta GP, Nanda UN, Saikisshore V. Design, development and In vivo evaluation of core in cup tablets of budesonide. Research Journal of Pharmacy and Technology. 2022;15(10):4553-8.DOI- 10.52711/0974-360X.2022.00764
4. Patil S, Rakshe A, Jagtap R, Jagtap S. Press coated bioadhesive pulsatile tablet of lisinopril for chronotherapy of cardiac disorders: In-vitro evaluation. Research Journal of Pharmacy and Technology. 2022;15(7):3057-62. DOI- 10.52711/0974-360X.2022.00511
5. Ramarao CT, Madhuri S. In-vitro Design and Formulation of Levitiracetam Extended Release Tablets. Research Journal of Pharmacy and Technology. 2022;15(8): 3681-4.DOI-10.52711/0974-360X.2022.00617
6. Prusty A, Gupta BK, Mishra A. Formulation and In vivo evaluation of pharmacokinetics parameters of extended-release matrix tablet containing drug benidipine hydrochloride by using PK solver software. Research Journal of Pharmacy and Technology. 2022;15(11): 4924-30.DOI- 10.52711/0974-360X.2022.00827
7. Kumari PV, Rao YS, Akhila S, Sindhu KB. Design and characterization of orlistat bilayered controlled release tablets. Research Journal of Pharmacy and Technology. 2021;14(6): 2976-82.DOI-10.52711/0974-360X.2021.00521

8. Shinde AJ, Khandekar SS, Bhatia MS, Tamboli FA, Jarag RJ, More HN. Comparative evaluation of formulations designed using chemically modified pectin and eudragit for sustained release of nateglinide. Research Journal of Pharmacy and Technology. 2023;16(12): 5775-81.DOI-10.52711/0974-360X.2022.00827
9. Lavhate KS, Solunke RS, Kore KJ, Shete RV, Deshmukh MT. Development and Characterization of Mesalamine Microsphere for Colon Specific Drug Delivery. Research Journal of Pharmacy and Technology. 2020;13(4): 1747-51.DOI-10.5958/0974-360X.2020.00315.7
10. Afokoghene AJ, Daguo A. Formulation and Evaluation of Controlled Release Theophylline Tablets using Grewia spp Gum as Binder. Research Journal of Pharmacy and Technology. 2022;15(6):2697-702.DOI- 10.52711/0974-360X.2022.00451
11. Chowdary SK, Napoleon AA. Review of extended drug delivery oral formulations. Research Journal of Pharmacy and Technology. 2024;17(4):1916-24.DOI-10.52711/0974-360X.2022.00764
12. Bhattacharjee S, Guha N, Dutta G, Chakraborty M, Jana M, Paul S. Formulation and Evaluation of Sustained Release Matrix Tablet of Anti-Amoebic Drug by Natural Polymers. Research Journal of Pharmacy and Technology. 2017;10(7):2041-6.DOI-10.5958/0974-360X.2017.00356.0
13. Shukla AK, Bishnoi RS, Kumar M, Jain CP. Development of natural gum based sustained release tablets of propranolol hydrochloride. Research Journal of Pharmacy and Technology. 2019;12(7):3295-300.DOI- 10.5958/0974-360X.2019.00546.8
14. Mariz M, Murta J, Gil MH, Ferreira P. An ocular insert with zero-order extended delivery: release kinetics and mathematical models. European Journal of Pharmaceutics and Biopharmaceutics. 2022 Dec 1;181:79-87.DOI-10.1016/j.ejpb.2022.10.023
15. Zhang R, Shi H, Li S, Zhang H, Zhang D, Wu A, Zhang C, Li C, Fu X, Chen S, Shi J. A double-layered gastric floating tablet for zero-order controlled release of dihydromyricetin: Design, development, and in vitro/in vivo evaluation. International Journal of Pharmaceutics. 2023 May 10;638:122929.DOI-/10.1016/j.ijpharm.2023.122929
16. Umasankar K. Formulation, design, and evaluation of valsartan sodium-sustained-release matrix tablets. The Journal of Multidisciplinary Research. 2024 Jun 22:1-3.DOI-10.37022/tjmdr.v4i2.577
17. Laracuente ML, Marina HY, McHugh KJ. Zero-order drug delivery: State of the art and future prospects. Journal of Controlled Release. 2020 Nov 10;327:834-56.DOI-10.1016/j.jconrel.2020.09.020
18. Wang M, Ge RL, Zhang F, Yu DG, Liu ZP, Li X, Shen H, Williams GR. Electrospun fibers with blank surface and inner drug gradient for improving sustained release. Biomaterials advances. 2023 Jul 1;150:213404.DOI-10.1016/j.bioadv.2023.213404
19. .Kaur S, Sivasankaran S, Wambolt E, Jonnalagadda S. Determinants of zero-order release kinetics from acetaminophen-layered Suglet® pellets, Wurster-coated with plasticized Aquacoat® ECD (ethyl cellulose dispersion). International Journal of Pharmaceutics. 2020 Jan 5;573:118873.DOI-10.1016/j.ijpharm.2020.119397
20. Kaur S, Sivasankaran S, Wambolt E, Jonnalagadda S. Determinants of zero-order release kinetics from acetaminophen-layered Suglet® pellets, Wurster-coated with plasticized Aquacoat® ECD (ethyl cellulose dispersion). International Journal of Pharmaceutics. 2020 Jan 5;573:118873.DOI-10.1016/j.ijpharm.2019.118873
21. 21.Venkatesh DN, Meyyanathan SN, Shanmugam R, Zielinska A, Campos JR, Ferreira JD, Souto EB. Development, in vitro release and in vivo bioavailability of

sustained release nateglinide tablets. Journal of Drug Delivery Science and Technology. 2020 Feb 1;55:101355.DOI-10.1016/j.jddst.2019.101355
22. Nguyen TT, Hwang KM, Kim SH, Park ES. Development of novel bilayer gastroretentive tablets based on hydrophobic polymers. International Journal of Pharmaceutics. 2020 Jan 25;574:118865.DOI-10.1016/j.ijpharm.2019.118865
23. Subramani M, Vekatashwaramurthy N, Sambathkumar R. A Novel Approach on Role of Polymers Used in Sustained Re-lease Drug Delivery System—A Review. Saudi J. Med. Pharm. Sci. 2021;7:170-8.DOI- 10.36348/sjmps.2021.v07i04.002
24. Bakre LG, Akinyele E, Bamiro O, Adeleye O, Kunle O. Formulation and evaluation of sustained release ibuprofen matrix tablets using starch from maize genotypes as polymer. Acta Marisiensis-Seria Medica. 2021 May 31;67(2):122-6.DOI-10.2478/amma-2021-0018
25. Buddhadev SS, Garala KC, Buddhadev S. Formulation and Evaluation Of Sustain Release Matrix Based Tablet Of Ketorolac Tromethamine Using Tamarind Gum and Tapioca Starch Natural Polymers As Release Modifiers. Educational Administration: Theory And Practice. 2024 May 30;30(6(S)): 144-54.DOI-10.1016/j.ijpharm.2016.11.067
26. Prajapati PH, Nakum VV, Patel CN. Formulation and evaluation of floating matrix tablet of stavudine. International Journal of pharmaceutical investigation. 2012 Apr;2(2):83.DOI-10.4103%2F2230-973X.100047.
27. Tarke Santosh R, Palani Shanmugasundaram. Formulation and evaluation of fast Dissolving tablets ofAntihypertensive Drug. Research J. Pharm. and Tech. 2017; 10(1): 155-160.
28. Tarke Santosh R , P. Shanmugasundaram. Antioxidant and Hepatoprotective activity of Ehretia laevis Roxb against paracetamol induced acute Hepatotoxicityin wistar rats. Research J. Pharm. and Tech. 2019; 12(12): 6143-6148.
29. Tarke Santosh R, P. Shanmugasundaram. Evaluation of hepatoprotective and anticancer potential of Ehretia laevis: An In-vitro evidence. Research J. Pharm. and Tech. 2019; 12(11):5467-5471.
30. Tarke Santosh R and Dr. P. Shanmugasundaram. GC-MS analysis of ethanolic extract of Ehretia laevis Roxb . J Pharmacogn Phytochem 2018;7(6):801-803.
31. Tarke Santosh R and Dr. P. Shanmugasundaram. Preliminary phytochemical screening and HPTLC method for qualitative determination of phytochemical compounds in extract of Ehretia laevis Roxb. J Pharmacogn Phytochem 2018;7(6):867-874.
32. Waman Rahul Laxman and Mansuk Avinash Gorakh, Antibiotics Resistance- Global Threat to Public Health, World Journal of Pharmacy & Pharmaceutical Sciences. 2024, Vol 13, Issue 3, 250-256.
33. Ranajit Damodhar Tijare, Vinod Shinde, Ambika Nagarbhadiya, Abhijeet Pohekar, Snehal Sambhaji Gadhave, Kirankumar Dhawale, Rahul Laxman Waman and Mansuk Avinash Gorakh. In vivo antioxidant activity of polyherbal combination using Ashwagandha and shakhotaka alcohol extracts: a novel approach. Journal of Clinical Otorhinolaryngology, Head, and Neck Surgery, 2023, 27 (2), 2920 – 2930.
34. N. S. Gallani, Dr. S. J. Dighade, Prof Waman Rahul Laxman, Dr Mansuk Avinash Gorak, Padekar Chetana Arjun, Navale Sonali Uttam, Shirtar Sushma Gorak, Jagtap Prajakta Sambhaji, Formulation And Evaluation Of Topical Gel Loaded With Ibuprofen Microsponges. 2024; 44(03), 6720-6738.
35. MRP Rao, S Taktode, SS Shivpuje, S Jagtap. Optimization of Transmucosal Buccal Delivery of Losartan Potassium using Factorial Design. Indian Journal of Pharmaceutical Education and Research, 2016; 50(2): S132-S139.

36. N Patre, S Patwekar, S Dhage, S Shivpuje. Formulation & Evaluation Of Piroxicam Bionanocomposite For Enhancement of Bioavailability. European Journal of Molecular & Clinical Medicine, 2020; 7(11): 9362-9376.
37. SJ Wadher, SL Patwekar, SS Shivpuje, SS Khandre, SS Lamture. Stability Indicating Assay Methods for Simultaneous Estimation of Amoxicillin Trihydrate And Cloxacillin Sodium in Combined Capsule Dosage Form by UV-Spectrophotometric Method. European Journal of Biomedical and Pharmaceutical sciences, 2017; 4(10): 858-864.
38. Santosh A. Payghan Shivraj S. Shivpuje Shailesh L. Patwekar, Karna B. Khavane, Padmavati R. Chainpure. A Review on Different Preparation Method Used For Development of Curcumin Nanoparticles. International Journal of Creative Research Thoughts, 2021;9(1):4088-4101.
39. Zeba Ashfaq Sheikh P. R. Chainpure, S. L. Patwekar, S. S. Shivpuje. Formulation and evaluation of Garciniacambogia and Commiphoramukul Herbal tablets used for AntiObesity. International Journal of Engineering, Science and Mathematics, 2019; 8(4): 180-195.
40. Pravin P Karle, Shashikant C Dhawale, Vijay V Navghare, Shivraj S Shivpuje. Optimization of extraction conditions and evaluation of Manilkara zapota (L.) P. Royen fruit peel extract for in vitro α-glucosidase enzyme inhibition and free radical scavenging potential. Future Journal of Pharmaceutical Sciences, 2021; 7(1):1-10.
41. Sheetal Rathod P. R. Chainpure, S. L. Patwekar, S. S. Shivpuje. A Study Of Carica Papaya Concerning It's Ancient And Traditional Uses - Recent Advances And Modern Applications For Improving The Milk Secretion In Lactating Womens. International Journal of Research, 2019;8(2):1851-1861.
42. Shivraj S. Shivpuje Shailesh J. Wadher, Bhagwan B. Supekar. Development And Validation Of New Ft-Ir Spectrophotometric Method For Simultaneous Estimation Of Ambroxol Hydrochloride And Cetirizine Hydrochloride In Combined Pharmaceutical. International Research Journal of Pharmacy, 2019; 10(3):110-114.
43. Shivraj S. Shivpuje, Shailesh J. Wadher, Bhagwan B. Supekar. Simultaneous Estimation of Ambroxol Hydrochloride and Cetirizine Hydrochloride in Combined Solid Tablet Formulations by HPTLC- Densitometric Method. Asian Journal of Biochemical and Pharmaceutical Research, 2019; 9(1):1-10.
44. JW Sailesh, SS Shivraj, SI Liyakat. Development and Validation of Stability Indicating RP-HPLC Method for the Estimation of Simvastatin in Bulk and Tablet Dosage form. Research Journal of Pharmacy and Technology, 2018; 11(4): 1553-1558.
45. Patil S. S. Shivpuje Shivraj S. Patre Narendra G. Development and Validation Of Stability Indicating HPTLC Method For Determination of Nisoldipine (Niso) In Tablet Dosage Form. European Journal of Biomedical and Pharmaceutical sciences, 2017; 4(12):462468.
46. W Shailesh, K Tukaram, S Shivraj, L Sima, K Supriya. Development and Validation of Stability Indicating UV Spectrophotometric Method for Simultaneous Estimation of Amoxicillin Trihydrate and Metronidazole In Bulk And In-House Tablet. World Journal of Pharmaceutical and Medical Research, 2017;3(8):312-318.
47. J Wadher Shailesh, M Kalyankar Tukaram, S Shivpuje Shivraj. Development and Validation of Stability Indicating Assay Method for Simultaneous Estimation of Amoxicillin Trihydrate and Cloxacillin Sodium In Pharmaceutical Dosage Form By Using RP-HPLC. World Journal of Pharmaceutical Research, 2017; 10(6):1002-1006.
48. Shital S. Sangale, Priyanka S. Kale, Rachana B. Lamkane, Ganga S. Gore, Priyanka B. Parekar, Shivraj S. Shivpuje (2023). Synthesis of Novel Isoxazole Derivatives as

Analgesic Agents by Using Eddy's Hot Plate Method. South Asian Res J Pharm Sci, 5(1): 18-27.

49. Priyanka B. Parekar, Shivraj S. Shivpuje, Vijay V. Navghare, Manasi M. Savale, Vijaya B. Surwase, Priti S. Mane- Kolpe, Priyanak S. Kale. Polyherbal Gel Development And Evaluation For Antifungal Activity, European Journal of Molecular & Clinical Medicine. 2022; 9(03): 5409-5418.
50. Jain AA, Mane-Kolpe PD, Parekar PB, Todkari AV, Sul KT, Shivpuje SS. Brief review on Total Quality Management in Pharmaceutical Industries, International Journal of Pharmaceutical Research and Applications. 2022; 7(05):1030-1036.
51. Sumaiyya. K. Attar, Pooja P. Dhanawade, Sonali S. Gurav , Prerna H. Sidwadkar , Priyanka B. Parekar, Shivraj S. Shivpuje. Development and Validation of UV Visible Spectrophotometric Method for Estimation of Fexofenadine Hydrochloride in Bulk and Formulation, GIS SCIENCE JOURNAL. 2022; 9(11): 936-944.
52. Sumayya Kasim Atar, Priyadarshini Ravindra Kamble, Sonali Sharad Gurav, Pooja Pandit Dhanawade, Priyanka Bhanudas Parekar, Shivraj Sangapa Shivpuje. Phytochemical Screening, Physicochemical Analysis of Starch from Colocasia Esculenta, NeuroQuantology, 2022; 20(20): 903-917.
53. Priti D.Mane-Kolpe, Alfa A. Jain, Tai P. Yele, Reshma B. Devkate, Priyanka B. Parekar, Komal T. Sul, Shivraj S. Shivpuje. A Systematic Review on Effects of Chloroquine as a Antiviral against Covid-19, International Journal of Innovative Science and Research Technology, 2022;7(11): 989-995.
54. Dr. Rohit Jadhav, Prof. Abhay D. Kale, Dr. Hitesh Vishwanath Shahare, Dr. Ramesh Ingole, Dr Shailesh Patwekar, Dr S J Wadher, Shivraj Shivpuje. Molecular Docking Studies and Synthesis of Novel 3-(3- hydroxypropyl)-(nitrophenyl)[1,3] thiazolo [4,5-d] pyrimidin2(3H)-one as potent inhibitors of P. Aeruginosa of S. Aureus, Eur. Chem. Bull. 2023; 12(12): 505-515.
55. Priyanka B. Parekar, Savita D. Sonwane, Vaibhav N. Dhakane, Rasika N. Tilekar, Neelam S. Bhagdewani, Sachin M. Jadhav, Shivraj S. Shivpuje, Synthesis and Biological Evaluationof Novel 1,3,4-Oxadiazole Derivatives as Antimicrobial Agents, Journal of Cardiovascular Disease Research, 2023; 14(8):611-624.
56. Kavita R. Mane, Prachi A. Ghadage, Aishwarya S. Shilamkar, Vaishnavi A. Pawar, Sakshi B. Taware, Priyanka B. Parekar, Shivraj S. Shivpuje. Phytochemical Screening, Extraction and In-vivo study of Immunomodulation effect of Withania somnifera, Momordicadioica and Annonasqumosa leaves. Journal of Cardiovascular Disease Research, 2023; 14(9): 231-241.
57. Harshada S. Deshmukh, Vishal B. Babar, Prajkta S. Jagtap, Rupendra V. Doshi, Shivarti V. Deokate, Ashwini V. Todkari, Amrata S. Mantri, Priyanka B. Parekar, Shivraj Shivpuje (2024). A Comprehensive Review Article on Herbal Cosmetics. South Asian Res J Pharm Sci, 6(3): 50-68.