"Development And Assessment of Immediate Release Nitrofurantoin Tablet and Sustained Release Trimethoprim Tablet: Formulation, Characterization and Comparative Evaluation"

Vaibhav Ghansham Kute[1*], Dr. Manmeet Singh[2]

[1]*Ph.D Scholar, Department of Pharmaceutics, SunRise University, Alwar, Rajasthan, India.*

[2]*Ph.D Research Guide & Professor, Department of Pharmaceutics, SunRise University, Alwar, Rajasthan, India.*

***Corresponding author:** Vaibhav Ghansham Kute*

**Ph.D Scholar, Department of Pharmaceutics, SunRise University, Alwar, Rajasthan, India. E-mail: vaigkute@gmail.com*

ABSTRACT: The research includes an examination of material properties, an investigation into the compatibility of the drug and excipients, the development of analytical techniques, and the determination of tablet production methods for immediate and sustained release layers. The methodology for material characterization encompassed the analysis of the pharmaceuticals' solubility in various aqueous solutions and buffers. The evaluation of the compatibility between excipients and medications was conducted utilizing FT-IR spectroscopy. Furthermore, calibration curves were devised by the research team for Nitrofurantoin and Trimethoprim, enabling the quantification of these pharmaceutical substances via UV spectrophotometry. The preparation of the tablets involved the utilization of direct compression and moist granulation methods, respectively, for the immediate and sustained release layers. This required the application of a variety of excipients and polymers. The tablets underwent a thorough evaluation in a controlled laboratory environment, which encompassed assessments of their dimensions, resistance to deformation, mass variability, and susceptibility to fracturing, concentration of active component, breakdown time, and solubility. The findings demonstrated that the regression coefficients in the calibration curves were substantial, thereby validating the accuracy of the drug concentration estimations. The results of the solubility studies indicate that Nitrofurantoin becomes more soluble in acidic environments. However, it should be noted that the solubility of both Trimethoprim and Nitrofurantoin is influenced by various solvents and buffers. An investigation into the compatibility of pharmaceuticals and the excipients was conducted through the utilization of FT-IR spectroscopy to ascertain such compatibility or interaction. A micromeritics analysis of granule flow parameters unveiled batch-specific variations in flow characteristics which will impact the manufacturing procedure. Upon scrutinizing the tablets, discrepancies in multiple measurements were discovered among various samples, suggesting the possibility of atypical tablet characteristics. Nitrofurantoin and Trimethoprim exhibited a progressive release from their tablets over time in various samples, as indicated by the drug release profiles observed in vitro; this suggests that the tablets have distinct release kinetics. Nevertheless, the medication release data exhibited irregularities in its presentation, such as sporadic inputs, absent values, and potentially erroneous statistics. The presence of these inconsistencies has the potential to compromise the dependability and comprehension of the results. In brief, the research provides extensive knowledge regarding the development, examination, and assessment of Nitrofurantoin rapid release tablets and Trimethoprim sustained release tablets.

Keywords: Formulation, Drug Delivery, Comparative Evaluation, Excipient Compatibility, Tablet Characterization, Solubility Studies, Flow Properties, Drug Release Kinetics

1. INTRODUCTION

The current emphasis of pharmaceutical research lies in the progress and assessment of immediate release Nitrofurantoin tablets and sustained release Trimethoprim tablets. The goal is to enhance medication delivery systems to get superior therapeutic outcomes. Although there have been notable advancements in pharmaceutical formulations, there is still a noticeable lack of study in comprehensively understanding and evaluating these particular medication formulations.[1-2]

The present literature lacks a thorough comparative evaluation of immediate-release Nitrofurantoin and sustained-release Trimethoprim tablets, since previous research have mostly concentrated on particular medication formulations. This research gap necessitates a thorough examination of the formulation, material characterization, and assessment of these tablets. This examination will delve into their solubility patterns, compatibility with excipients, and release kinetics [3-4]

In addition, while some studies have examined the compatibility of medications and excipients using various techniques, there is a lack of comprehensive research that utilizes FTIR spectroscopy to evaluate the interactions between these pharmaceuticals and their respective excipients in the context of a formulation.[5-6]

Comprehending the rheological characteristics of granules and their influence on the process of manufacturing is crucial in order to guarantee the constant manufacture of tablets. However, there is a scarcity of information on the possible flow problems that may arise in various batches of Nitrofurantoin immediate-release and Trimethoprim sustained-release formulations. [7-8]

This research seeks to address these deficiencies by conducting a comprehensive investigation of the formulation, analysis, and evaluation of Nitrofurantoin tablets designed for rapid release, as well as Trimethoprim tablets intended for sustained release. This study seeks to rectify the discrepancies in the current body of literature by conducting a comprehensive evaluation and analysis of these formulations. By doing so, it hopes to fill the existing research gap and make a substantial contribution to the area of pharmaceuticals.

MATERIALS AND METHODS:

Analysis of IR/SR Granules:

The pharmaceutical compounds underwent rigorous solubility assessments across a spectrum of aqueous solutions and buffers to ascertain their dissolution characteristics. Assessments of drug-excipient compatibility were performed employing Fourier Transform Infrared Spectroscopy (FTIR). The granules constituting both the instant release (IR) and sustained release (SR) layers underwent comprehensive evaluations under diverse pre-compression settings. Through the utilization of the fixed funnel methodology, a precise determination of the angle of repose was successfully achieved. Additionally, the bulk and tapped densities were meticulously determined utilizing specialized equipment for tapped density measurement. [9-10]

The scanning procedure encompassed a spectral range of 4000 to 400 inverse centimeters and was iterated 20 times at a rate of 2 millimeters per second, maintaining a resolution of 4 centimeters per inverse centimeter. The obtained scan data were thoroughly scrutinized to ascertain the primary drug peaks, identify any positional shifts or distortions in these peaks, and observe the emergence of any additional peaks resulting from interactions with the employed polymers [11-12].

The development of analytical methods involved the calibration curve development process. Nitrofurantoin solutions with varying strengths, spanning from 2 to 10 μg/ml, were meticulously prepared by dilution with 0.1 N HCl. Utilizing a UV spectrophotometer (Shimadzu, India, UV-1700), the absorbance at λmax (282 nm) was precisely measured. Meanwhile, concentrations of Trimethoprim ranging from 2 to 10 μg/ml were determined by diluting with 0.5% w/v SLS. These concentration data were systematically correlated with their corresponding absorbance values to generate a conventional graph [13].

Procurement of drug:

Nitrofurantoin and Trimethoprimhave been obtained/procured from IPCA Mumbai.

The Immediate Release layer of Nitrofurantoin:

Using the direct compression approach, the Nitrofurantoin Immediate Release layer (F1-F9) was painstakingly created. After being measured and sieved using a #40 mesh sieve, the exact amounts of sodium starch glycolate, nitrofurantoin, crospovidone, croscarmellose sodium, and sodium lauryl sulfate were obtained. These materials were then carefully combined and placed into a polybag, with Table 2 presenting detailed data for these formulations. To make sure the powders were of the same size, they were mixed well for about 5 minutes and then re-sifted through a #40 sieve. [14-15].

Sustained Release layer of Trimethoprim:

To produce the Sustained Release layer (F1-F9) of Trimethoprim, a moist granulation method was utilized. A binding agent was employed, which consisted of an isopropyl alcohol solution containing 5% PVP K 30. The proprietary formulations employed are detailed in Table 2. The concentrations of mannitol, microcrystalline cellulose, ethyl cellulose, guar gum, xanthan gum, and HPMC E 15 were determined with precision by sifting them through a #40 micron sieve. Following thorough blending, the binding agent was applied progressively until the desired cohesion was achieved. To obtain the granules, the resultant substance was sieved through a #20 mesh. Subsequently, the granules were dried in a hot air oven set at 50ϽC until they were completely desiccated. In order to promote lubrication, magnesium stearate was applied uniformly to the desiccated particles. In addition, the talc and granules were combined through vigorous agitation. In order to compress tablets, a tablet compression machine was utilized, which consisted of ten stations and a 9 mm pierce size. As the sustained release polymer, HPMC E15 was utilized for batches N1-N3, whereas guar gum was employed for batches N4-N7. Batch N8 incorporated Xanthan gum into its composition, whereas Batch N9 utilized a blend of HPMC E15 and Guar gum. Batch N13 utilized a mixture of xanthan gum and guar gum, while Batch N10-N12 utilized a mixture of guar gum and ethyl cellulose. After a comprehensive blending period of around 5 minutes, the filtered granules were re-screened through a #40 sieve in order to guarantee consistent particle dimensions. After the powder mixture had been filtered through a #40 filter, magnesium stearate was introduced as a lubricant. In order to ensure color uniformity, a 0.125 w/w solution of iron oxide red, which had been filtered via a #100 sieve, was carefully combined. [16-17].

Table 1: Formulation of rapid-release Layer

Formulation	Ingredients in mg / tablet							
	Nitrofurantoin	MCC	CP	CCS	SSG	Mg . stearate	SLS	Fe_2O_3
F1	10	131	7.5	-	-	1.5	-	q.s.
F2	10	123.5	15	-	-	1.5	-	q.s.
F3	10	131	-	7.5	-	1.5	-	q.s.
F4	10	123.5	-	15	-	1.5	-	q.s.
F5	10	131	-	-	7.5	1.5	-	q.s.
F6	10	123.5	-	-	15	1.5	-	q.s.
F7	10	119.5	-	-	18.75	1.5	-	q.s.
F8	10	131	-	-	7.5	1.5	0.3	q.s.
F9	10	123.5	-	-	15	1.5	0.3	q.s.

In this context, sodium starch glycolate (SSG), microcrystalline cellulose (MCC), crospovidone (CP), croscarmellose sodium (CCS), and sodium lauryl sulfate (SLS) are all used.

Table 2: Elements comprising the sustained release layer

Ingredients	F1	F2	F3	F4	F5	F6	F7	F8	F9
Trimethoprim	60	60	60	60	60	60	60	60	60
HPMC	30	45	60	-	-	-	-	-	45
Guar gum	-	-	-	30	45	60	75	-	-
X - gum	-	-	-	-	-	-	-	75	45
MCC	180	165	150	180	165	150	135	135	120
Mg .st .	7.5	7.5	7.5	7.5	7.5	7.5	7.5	7.5	7.5
Mannitol	-	-	-	-	-	-	-	-	-
PVP	15	15	15	15	15	15	15	15	15
Talc	7.5	7.5	7.5	7.5	7.5	7.5	7.5	7.5	7.5
Total weight	300	300	300	300	300	300	300	300	300

Hydroxypropyl methyl cellulose (HPMC), Xanthan gum (X-gum), ethyl cellulose (EC), and microcrystalline cellulose (MCC) are some of the terms used in this context. The acronyms "Mg. st." and "PVP" stand for magnesium stearate and polyvinyl pyrrolidone, respectively.

Evaluating SR and IR Tablets for Fast and Delayed Release:

A thorough evaluation was conducted on both SR and IR tablets, comprising a multitude of parameters in order to ascertain their quality and efficacy. A variety of assessments were performed, encompassing evaluations of tablet rigidity, thickness, variation in weight, friability, and uniformity of drug content. The pressure resistance of six tablets was evaluated by subjecting them to a Monsanto hardness test, which determined their hardness. The unit of measurement for this assessment was kilograms per square centimeter. The weight variation of each of the twenty tablets was carefully assessed individually. The average weight, mean, and standard deviation were computed to ensure adherence to dosage accuracy standards that had been predetermined.

The purpose of the friability testing was to ascertain the extent of material degradation caused by abrasion. Tablets that had been pre-weighed were subjected to a series of shocks using a Roche friabilator. The tablets' initial mass ($\boldsymbol{L}0$) was documented, after which they were inserted into a rotating cylinder and discharged from a height of 6 inches to simulate the motion of tumbling. The tablets underwent a reweighing process (W) following 100 rotations, which enabled the computation of percentage weight loss or friability (a) utilizing the formula provided.

It is imperative to acknowledge that the text provided contains allusions to numerical values (specifically, nineteen and twenty-two), which may serve as placeholders or have no direct bearing on the procedures being described. For the purpose of ensuring coherence in the context of tablet evaluation, these should be reviewed or clarified.

$$\%\text{Friability} = \frac{\text{Initial weight} - \text{Final weight}}{\text{Initial weight}} \times 100. \quad (1)$$

Pharmaceutical information:
The pharmaceutical constituents of the tablets were ascertained via a series of rigorous procedures. Following the calculation of the mean weight of twenty tablets, the tablets were subsequently reduced to a powdery consistency using a mortar. A precise quantity equal to the mean weight of the tablets was determined and subsequently poured into a 100 mL volumetric vial. In order to achieve the intended solubility of the substance, a minute amount of methanol was introduced, and the volume was modified using a suitable medium. Consistently stirring the solution for duration of one hour while leaving it undisturbed guaranteed the thorough dissolution of the medication. After the solution was dissolved, it was filtered and the required dilutions were prepared. By establishing the permissible range for drug content as 90% to 110% of the standard drug content level, it was possible to guarantee that the tablets adhered to pre-established criteria. [21-22]

Disintegrating Time:
The disintegration test was conducted using a device produced by the Mumbai-based Electro Lab. The instrument consists of a basket rack that accommodates six glass tubes, with each tube having a diameter of 2.15 mm and a length of 7.75 cm. Each tube contains a sieve situated at the lowermost section, featuring a grain size that corresponds to #10. The container rotates between 28 and 32 times per minute in a cyclical pattern comprised of ascending and descending motions. In order to conduct the experiment, six tablets were positioned in individual glass tubes, and the exact time it took for the tablet fragments to traverse the lattice (#10) was precisely timed. The aforementioned period was deemed to be the time required for the disintegration of the tablet and was documented as such. Furthermore, the duration required for the tablet to completely dissolve was monitored and recorded as an integral component of the experiment. [23-24]

In vitro dissolution studies:
The drug release characteristics of multiple samples of manufactured tablets were assessed using a USP type II dissolution apparatus. The assessment procedure incorporated two separate disintegrating fluids: to begin with, 500 ml of 0.1 N hydrochloric acid (HCl) was utilized for the initial thirty minutes in order to expedite the release from the immediate release layer. In order to maintain consistency, the volume that was gathered was refilled with new media at predetermined time intervals, and subsequent samples were collected in a corresponding manner. After subjecting each sample to filtration through Whatman filter paper, precise max values were determined for each sample using a spectrophotometer. Subsequently, a comparison was conducted between the samples and a blank medium.[25-26]

RESULTS AND DISCUSSION:
Development of Analytical Methods:
Using data gathered from a UV spectrophotometer, calibration curves were created for trimethoprim and Nitrofurantoin. The regression coefficients for the two medications were 0.9996 and 0.9999, respectively, as seen in these graphs.

Development of Calibration Curve:

Table 3: Calibration curve data for Nitrofurantoin in a 0.1 N hydrochloric acid solution

Concentration (ug/ml)	The unit of absorbance (nm)
0	0
2	0.072
4	0.146
6	0.219
8	0.289
10	0.352

Table 4: Calibration curve for Trimethoprimin in a solution containing 0.1% N hydrochloric acid and 0.5% w/v sodium lauryl sulfate (SLS).

Concentration (ug/ml)	The unit of absorbance (nm)
0	0

2	0.064
4	0.125
6	0.176
8	0.242
10	0.305

Solubility study:

The solubility study aimed to determine the solubility profiles of Nitrofurantoin and Trimethoprim in various solvents and buffers. The obtained data reveal distinct solubility patterns for the two compounds across different media.

Table 5: Analysis of the solubility of Nitrofurantoin and Trimethoprim in various solvents and buffers.

Name of buffer / solvent	Nitrofurantoin (mg/ml)	Trimethoprim (mg/ml)
Water	0.0016	0.002
Phosphate buffer pH 6.8	0.0011	0.022
Methanol	0.0813	0.343
DMSO	0.4566	0.575
HCl buffer pH 1.2	1.2233	0.106
PEG	0.9101	-

Nitrofurantoin and Trimethoprim showed different solubility profiles across different solvents and buffers, influenced by pH variations. Nitrofurantoin showed low solubility in water, but increased significantly in an acidic environment, indicating its potential for improved dissolution in acidic conditions. PEG showed a significant enhancement, suggesting its potential as a solubility enhancer. DMSO and methanol also showed moderate improvements in solubility. Trimethoprim had low solubility across most tested solvents and buffers, with water showing minimal solubility. DMSO showed higher solubility, suggesting its potential as a solvent for Trimethoprim. To make these medications more bioavailable and soluble, which is crucial for their effective therapeutic usage, the data suggest that pH-modifying agents and certain solvents may be able to do just that. To enhance their efficacy in clinical settings, more research and formulation improvement using these solvents and buffers are required.

Compatibility between drugs and excipients by employing Fourier Transform Infrared Spectroscopy

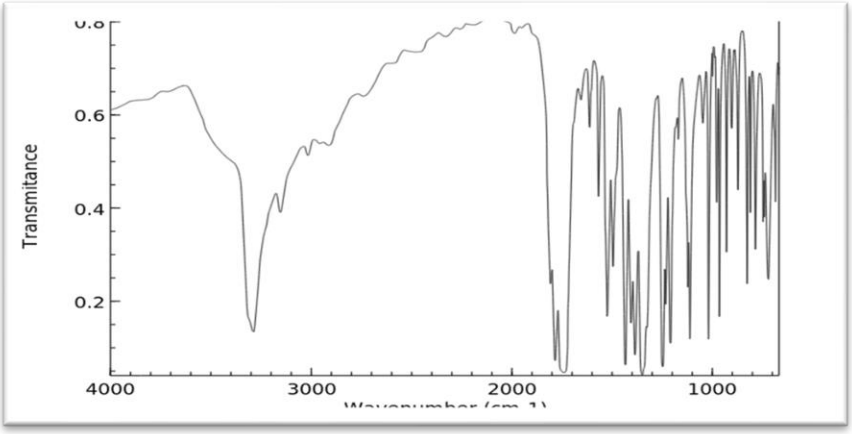

Figure 1: FTIR of Nitrofurantoin Pure drug

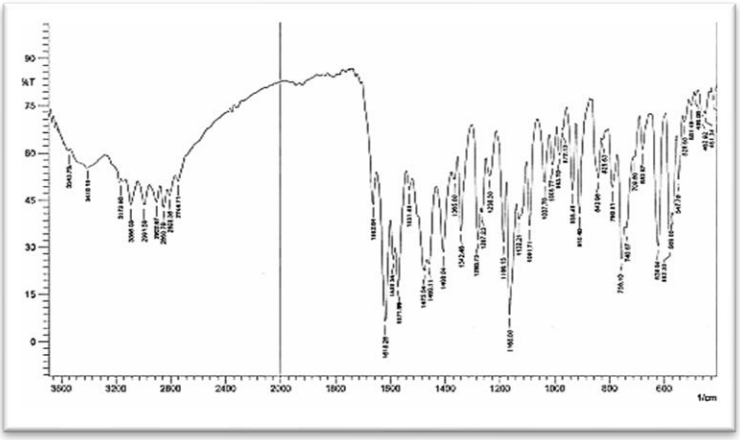

Figure 2: FTIR of Trimethoprim Pure drug

Micromeritics Studies:

A summary of data from multiple batches regarding the flow properties of the immediate release layer (Nitrox) and sustained release layer (Trimethoprim) is provided in the tables. The flow characteristics and manufacturability of the tablet formulations may be assessed in accordance with these criteria.

Table 6: Flow characteristics of the immediate release layer for Nitrofurantoin

Formulation	Angle of repose	Bulk density (g / cm³)	Tapped density (g / cm³)	Carr's index (%)	Hausner's ratio
F1	30.17	0.34	0.40	15.00	1.17
F2	34.70	0.35	0.47	25.53	1.34
F3	26.10	0.34	0.41	17.07	1.20
F4	29.12	0.34	0.40	15.00	1.17
F5	28.47	0.34	0.39	12.82	1.14
F6	26.96	0.35	0.43	18.60	1.22
F7	26.10	0.36	0.41	12.19	1.13
F8	27.92	0.35	0.42	16.66	1.20
F9	28.01	0.35	0.40	12.50	1.14

Table 7: The flow characteristics of the sustained-release layer of trimethoprim

Formulation	Angle of repose	Bulk density (gm / cm³)	Tapped density (gm / cm³)	Carr's index (%)	Hausner's
F1	34.11	0.31	0.36	13.52	1.0
F2	33.14	0.32	0.39	22.53	1.28
F3	32.17	0.33	0.39	10.52	1.02
F4	31.21	0.37	0.43	13.62	1.14
F5	33.79	0.31	0.34	14.23	1.18
F6	32.14	0.35	0.41	14.22	1.17
F7	31.00	0.28	0.32	12.18	1.23
F8	29.55	0.31	0.33	14.24	1.35
F9	28.50	0.32	0.34	11.41	1.15

Batches F2 and F6 have elevated angle of repose values (>30), suggesting a comparatively worse flowability in comparison to the other batches. In addition, batch F2 has a greater Carr's index (25.53%), indicating a lower level of homogeneity in the distribution of particle sizes. In general, differences in these factors across batches might affect the simplicity of manufacturing and the uniformity of the quick release layer.

Similarly, variations in flow characteristics are seen in various batches of the Trimethoprim sustained release layer. Batches F2 and F6 have elevated angle of repose values (>30), suggesting the presence of flowability concerns. Batch F2 specifically has a greater Carr's index (22.50%), suggesting a lower level of homogeneity in the distribution of particle sizes. The discrepancies between batches might impact the production process and consistency of the sustained release layer.

Evaluation of Sustained Release (SR) and Immediate Release (IR) Tablets:

The following tables provide an overview of the assessment criteria for Nitrofurantoin instant release tablets and Trimethoprim sustained release tablets in various batches.

Table 8: Nitrofurantoin instant release tablet evaluation criteria

Formulation	Weight fluctuation(%)	Hardness (kg / cm²)	Thickness (mm)	Friability (%)	Drug content (%)	Disintegration time (min)
F1	0.53	4.3	2.83	0.13	95.56	3.40
F2	1.19	4.5	3.29	0.15	97.20	2.55
F3	2.51	4.0	3.18	0.14	96.45	4.10
F4	1.19	5.0	3.30	0.13	90.84	3.28
F5	1.25	3.5	2.85	0.16	103.01	3.56
F6	3.18	4.3	2.91	0.12	97.62	2.45
F7	0.53	4.2	3.10	0.15	100.94	1.50
F8	1.25	4.5	3.05	0.18	98.19	3.45
F9	0.53	4.5	3.20	0.16	99.42	2.40

Table 9: Trimethoprim extended release tablets evaluation criteria.

Formulation	Weight fluctuation (%)	Hardness (kg / cm²)	Thickness (mm)	Friability (%)	Drug content (%)
F1	0.22	7.0	3.97	0.59	96.12
F2	0.89	5.8	3.95	0.62	97.45
F3	0.55	7.2	3.99	0.60	98.10
F4	1.55	6.8	3.85	0.54	95.53
F5	1.20	6.2	3.57	0.70	98.63
F6	0.89	5.5	3.84	0.69	98.84
F7	0.22	6.5	3.73	0.72	97.14
F8	0.22	5.5	3.69	0.54	101.15
F9	0.55	6.8	3.89	0.52	98.68

Critical characteristics of the Nitrofurantoin immediate-release tablets were assessed, including their ebb and flow, thickness, hardness, friability, medication content, and disintegration duration. Differences in weight fluctuation, hardness, and disintegration time are seen across different batches. Batches F3 and F6 exhibit greater weight fluctuations (2.51% and 3.18%, respectively), suggesting possible irregularities in tablet weight. The disintegration time varies across batches, ranging from 1.50 to 4.10 minutes. Furthermore, batch F5 has significantly elevated drug content (103.01%), necessitating further scrutiny for quality assurance purposes.

Trimethoprim sustained release tablets also vary in weight, hardness, thickness, friability, and drug content from batch to batch. Batch F8 has a significantly elevated drug content (101.15%), which has the potential to affect the consistency of dose administration. Furthermore, discrepancies in the hardness and thickness across batches indicate possible variances in the tablet compression and creation procedures.

Data on the release of Nitrofurantoin from instant release tablets in an artificial environment:

Each of the nine batches of Nitrofurantoin instant release tablets (F1–F9) was tested for their in vitro drug release profile at different time intervals ranging from zero to thirty minutes. The values in the table represent the cumulative drug release percentages (as a proportion of the total drug content) at various time intervals for each batch.

Table 10: In vitro drug release data of Nitrofurantoin immediate release tablets

Time	F1	F2	F3	F4	F5	F6	F7	F8	F9
0	0	0	0	0	0	0	0	0	0
5	11 + 3.12	16 +3.26	14 + 3.11	193.80	16 +3.57	19 +3.85	19 + 24	25+ 3.96	273.68
10	21 +3.45	28 + 3.40	25 +4.25	28 + 3.54	29 +4.20	32 + 3.15	31 +3.20	43 +3.56	41+ 3.24
15	35 +3.08	36 + 4.05	34 + 4.50	38 + 3.69	42 + 4.22	46 +4.12	48 +4.01	50 +3.94	58 +3.80
20	49 ± 4.15	50± 4.91	47 +3.75	52±4.52	58 +3.75	59 +3.46	60+ 4.23	66 +4.25	734.31
25	55 ±3.89	61 ± 3.89	53 +3.90	59 + 3.96	64 +3.58	66 + 4.29	70+ 3.99	80+ 3.98	883.78
30	64 ± 4.52	69 ± 3.68	65 + 4.82	68 +4.95	74 + 4.52	80+ 4.42	84 +4.58	96 ± 3.80	97 +3.94

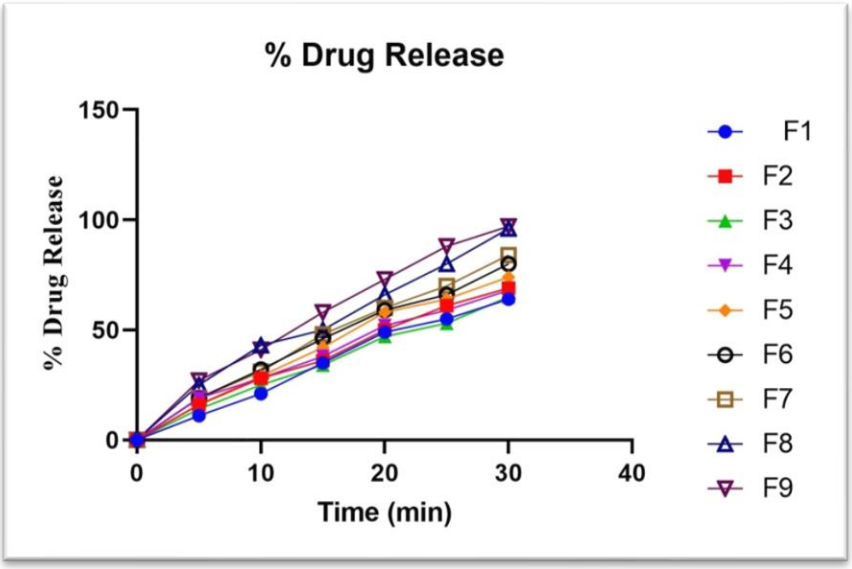

Figure 3: In vitro Nitrofurantoin instant release tablet drug release study

A comprehensive evaluation and verification of the data are essential to verify the accuracy and reliability of the results and to provide a precise interpretation and analysis of the drug release pattern of Nitrofurantoin instant release tablets across different batches and time intervals. In order to provide a dependable comprehension of the drug release behaviour for every batch of tablets, it is necessary to address and rectify any discrepancies or mistakes in note or recording.

Drug release data in vitro for sustained release granules of trimethoprim:

The table presents the outcomes of in vitro drug release assays conducted on Trimethoprim sustained release tablets at various time intervals (spanning from 0 to 12 hours) for batches F1 to F9. The values provided represent the cumulative percentages of drug discharge during each time period.

Table 11: In vitro drug release data of Trimethoprim sustained release tablets

Time (hrs)	F1	F2	F3	F4	F5	F6	F7	F8	F9
0	0	0	0	0	0	0	0	0	0
1	18 ± 3.99	14 + 3.45	16 + 3.51	29 ± 3.68	19 + 4.03	16 ± 4.02	15 + 3.38	10 ± 3.37	9 + 3.90
2	40+ 3.46	38 ± 4.14	28 + 4.07	38 ± 3.72	39 +3.72	32 ± 3.61	20+ 3.64	18+ 3.99	15 +3.68

3	56 + 3.14	59 ± 3.78	49 + 3.54	54 +3.58	48 ± 3.80	41 +3.94	31 + 437	26 + 3.42	26 ± 3.42
4	78 ± 4.44	72 ± 3.45	61 ± 3.92	79 ± 4.45	61 ± 4.19	59 ± 4.55	42 ± 4.11	37 ± 3.98	32 ± 4.20
5	85 +3.83	83 + 4.42	75 ± 3.96	94 +3.83	80+ 3.27	73 ± 3.93	53 ± 3.67	48 ± 3.71	39 ± 3.63
6	97 + 4.56	90+ 4.28	84 ± 3.52		95 ± 3.36	85 +4.19	61 ± 4.10	59 + 4.45	47 ± 3.06
7		95 ± 4.01	90 + 4.08			91 +3.40	69 3.36	65 +3.23	53 ± 3.67
8			96 + 3.81			98 ± 3.79	78 ± 3.44	78 +3.44	60 +3.27
9							97 ± 3.43	85 +3.87	75 + 4.14
10								98 ± 3.30	81 +3.74
11									92 + 3.48
12									96 ± 3.92

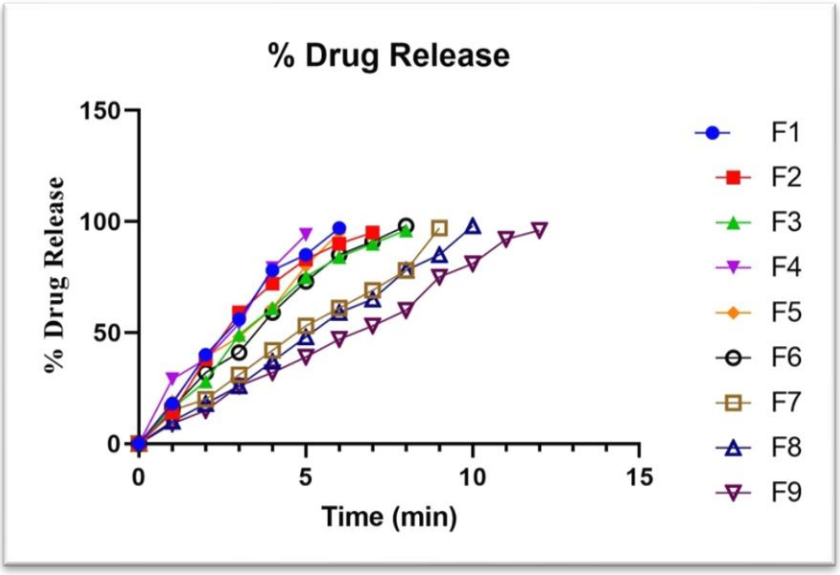

Figure 4: In vitro drug release profile of Trimethoprim sustained release tablets

The data seems to show that, across batches of sustained-release tablets, Trimethoprim is released gradually over time. However, to accurately interpret and analyze the drug release behaviour for each batch and draw reliable conclusions regarding sustained release characteristics, it's crucial to address any inconsistencies or missing information in the dataset. Verification and completion of the missing values or clarification regarding notation inconsistencies are necessary to ensure the accuracy and reliability of the findings.

CONCLUSION:

The study on immediate-release Nitrofurantoin tablets and sustained-release Trimethoprim tablets shows valuable insights into their formulation and characterization. The scope includes the analysis of material properties, investigation of drug-excipient interactions, creation of analytical methods, and comprehensive assessment of tablet compositions. Accurate calibration curves were constructed of Nitrofurantoin and Trimethoprim indicates precise drug concentration determination by using UV spectrophotometry. Solubility studies revealed Nitrofurantoin's enhanced solubility in acidic environments and the influence of pH variation on both drugs. Drug-excipient compatibility studies using FT-IR spectroscopy demonstrated potential interaction between drugs and their excipients; however, challenges in consistency among flow of granule properties across different batches indicates potential

manufacturability issues that need further optimization. Tablet evaluations showed variations among batches for various parameters, emphasizing the need for stringent quality control measures. Despite the comprehensive nature of the study, data inconsistencies were identified, potentially affecting the reliability and accuracy of the findings. Further optimization and refinement could enhance the quality and consistency of these pharmaceutical products for effective therapeutic use.

REFERENCES:

1. Lin, W., Li, Y., Shi, Q., Liao, X., Zeng, Y., Tian, W., Xie, X., & Liu, H. (2022). Preparation and evaluation of bilayer-core osmotic pump tablets contained topiramate. PloS one, 17(2), e0264457. https://doi.org/10.1371/journal.pone.0264457
2. Zhou, J., Wang, Y., & Jiang, G. (2020). Oxycodone versus morphine for cancer pain titration: A systematic review and pharmacoeconomic evaluation. PloS one, 15(4), e0231763. https://doi.org/10.1371/journal.pone.0231763
3. Jin, G., Ngo, H. V., Wang, J., Cui, J. H., Cao, Q. R., Park, C., Jung, M., & Lee, B. J. (2022). Design and evaluation of in vivo bioavailability in beagle dogs of bilayer tablet consisting of immediate release nanosuspension and sustained release layers of rebamipide. International journal of pharmaceutics, 619, 121718. https://doi.org/10.1016/j.ijpharm.2022.121718
4. Hassan, D. S., &Hasary, H. J. (2022). The impact of viscosity on the dissolution of naproxen immediate-release tablets. Journal of Taibah University Medical Sciences, 18(4), 687–695. https://doi.org/10.1016/j.jtumed.2022.12.009
5. Sun, Z., Yuan, S., Zhao, H., Wang, Z., & Liu, Z. (2017). Preparation and evaluation of 1-deoxynojirimycin sustained-release pellets vs conventional immediate-release tablets. Journal of microencapsulation, 34(3), 293–298. https://doi.org/10.1080/02652048.2017.1321694
6. Raza, A., Hayat, U., Wang, H. J., & Wang, J. Y. (2020). Preparation and evaluation of captopril loaded gastro-retentive zein based porous floating tablets. International journal of pharmaceutics, 579, 119185. https://doi.org/10.1016/j.ijpharm.2020.119185
7. Boozer, L. B., Platt, S. R., Haley, A. C., Linville, A. V., Kent, M., Barron, L. E., Nie, B., & Arnold, R. D. (2015). Pharmacokinetic evaluation of immediate- and extended-release formulations of levetiracetam in dogs. American journal of veterinary research, 76(8), 719–723. https://doi.org/10.2460/ajvr.76.8.719
8. Maddiboyina, B., Hanumanaik, M., Nakkala, R. K., Jhawat, V., Rawat, P., Alam, A., Foudah, A. I., Alrobaian, M. M., Shukla, R., Singh, S., &Kesharwani, P. (2020). Formulation and evaluation of gastro-retentive floating bilayer tablet for the treatment of hypertension. Heliyon, 6(11), e05459. https://doi.org/10.1016/j.heliyon.2020.e05459
9. Kwak, S. S., Lee, E. S., Yoon, H. Y., Kim, C. H., Goo, Y. T., Kang, M. J., Lee, S., Lee, B. S., Jeon, H. R., Oh, C. H., & Choi, Y. W. (2018). Immediate release tablet formulation of varenicline salicylate and comparative pharmacokinetic study in human volunteers. Drug design, development and therapy, 12, 3377–3392. https://doi.org/10.2147/DDDT.S178456
10. Tan, T., &Bunnapradist, S. (2021). Comparing the pharmacokinetics of extended-release tacrolimus (LCP-TAC) to immediate-release formulations in kidney transplant patients. Expert opinion on drug metabolism & toxicology, 17(10), 1175–1186. https://doi.org/10.1080/17425255.2021.1974399
11. Ibrahim, M., Sarhan, H. A., Naguib, Y. W., &Abdelkader, H. (2020). Design, characterization and in vivo evaluation of modified release baclofen floating coated beads. International journal of pharmaceutics, 582, 119344. https://doi.org/10.1016/j.ijpharm.2020.119344
12. Chavda, D., Joshi, D., Thakkar, V., & Gandhi, T. (2022). Fabrication and In Vitro Evaluation of Febuxostat Tablet for Obtaining Biphasic Drug Release Profile. Recent advances in drug delivery and formulation, 10.2174/2667387817666221116100127. Advance online publication. https://doi.org/10.2174/2667387817666221116100127
13. Gong, W., Liu, Y., Mei, D. Y., Yang, M., & Mei, X. G. (2015). Preparation, release and pharmacokinetics of a risperidone elementary osmotic pump system. Drug development and industrial pharmacy, 41(3), 464–469. https://doi.org/10.3109/03639045.2013.877923
14. Sundaramurthy, J. L., Natanasabapathy, V., Mahendran, K., Narasimhan, S., Raghu, S., Cherian, A. R., Vaanjay, M., &Krithikadatta, J. (2023). Efficiency of Immediate and Controlled release of Aceclofenac on Post-instrumentation Pain in Root Canal Treatment - A Triple Blind Randomized Controlled Trial. European endodontic journal, 8(2), 125–132. https://doi.org/10.14744/eej.2022.40469
15. Patil, H. G., Tiwari, R. V., Repka, M. A., & Singh, K. K. (2016). Formulation and development of orodispersible sustained release tablet of domperidone. Drug development and industrial pharmacy, 42(6), 906–915. https://doi.org/10.3109/03639045.2015.1088864
16. Eisenhauer, T. D., Matchett, M., Heasley, R., Morton, T., Devarakonda, K., Giuliani, M., Young, J. L., & Barrett, T. (2016). Evaluation of the tamper-resistant properties of biphasic immediate-release/extended-release oxycodone/acetaminophen tablets. Drug development and industrial pharmacy, 42(1), 157–165. https://doi.org/10.3109/03639045.2015.1038272

17. Li, N., Fan, L., Wu, B., Dai, G., Jiang, C., Guo, Y., & Wang, D. (2019). Preparation and in vitro/in vivo evaluation of azilsartan osmotic pump tablets based on the preformulation investigation. Drug development and industrial pharmacy, 45(7), 1079–1088. https://doi.org/10.1080/03639045.2019.1593441
18. Asnaashari, S., Khoei, N. S., Zarrintan, M. H., Adibkia, K., &Javadzadeh, Y. (2011). Preparation and evaluation of novel metronidazole sustained release and floating matrix tablets. Pharmaceutical development and technology, 16(4), 400–407. https://doi.org/10.3109/10837451003774393
19. Ölçer, M., Ölçer, A., İnce, İ., &Karasulu, E. (2015). Development and in vitro/in vivo evaluation of immediate release perindopril tablets. Pharmaceutical development and technology, 20(6), 684–693. https://doi.org/10.3109/10837450.2014.915568
20. Cascone S. (2017). Modeling and comparison of release profiles: Effect of the dissolution method. European journal of pharmaceutical sciences : official journal of the European Federation for Pharmaceutical Sciences, 106, 352–361. https://doi.org/10.1016/j.ejps.2017.06.021
21. Darwish, M. K. M., Abu El-Enin, A. S. M., & Mohammed, K. H. A. (2019). Formulation, optimization, and evaluation of raft-forming formulations containing Nizatidine. Drug development and industrial pharmacy, 45(4), 651–663. https://doi.org/10.1080/03639045.2019.1569033
22. Benabbas, R., Sanchez-Ballester, N. M., Aubert, A., Sharkawi, T., Bataille, B., &Soulairol, I. (2021). Performance Evaluation of a Novel Biosourced Co-Processed Excipient in Direct Compression and Drug Release. Polymers, 13(6), 988. https://doi.org/10.3390/polym13060988
23. NagasamyVenkatesh, D., Meyyanathan, S. N., Shanmugam, R., Kamatham, S. S., Campos, J. R., Dias-Ferreira, J., Sanchez-Lopez, E., Cardoso, J. C., Severino, P., &Souto, E. B. (2021). Physicochemical, pharmacokinetic, and pharmacodynamic characterization of isradipine tablets for controlled release. Pharmaceutical development and technology, 26(1), 92–100. https://doi.org/10.1080/10837450.2020.1839495
24. Dong, L., Yang, F., Zhu, Z., Yang, Y., Zhang, X., Ye, M., Pan, W., & Pan, H. (2018). Preparation, Characterization and Pharmacokinetics Evaluation of the Compound Capsules of Ibuprofen Enteric-Coated Sustained-Release Pellets and Codeine Phosphate Immediate-Release Pellets. AAPS PharmSciTech, 19(7), 3057–3066. https://doi.org/10.1208/s12249-018-1119-8
25. Mahmoud, E. A., Bendas, E. R., & Mohamed, M. I. (2009). Preparation and evaluation of self-nanoemulsifying tablets of carvedilol. AAPS PharmSciTech, 10(1), 183–192. https://doi.org/10.1208/s12249-009-9192-7
26. Gong, L., Sun, Y., Yu, M., Gao, Y., Zou, M., & Cheng, G. (2018). Development and Evaluation of Compression Coating Gastro-Floating Tablet of Alfuzosin Hydrochloride for Zero-Order Controlled Release. AAPS PharmSciTech, 19(7), 3277–3286. https://doi.org/10.1208/s12249-018-1168-z

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