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Formulation and In Vitro Evaluation of Paracetamol Sustained Release 1000 mg Tablets using Banana Starch As Dual-Action Control

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ABSTRACT

This study aimed to develop and evaluate sustained release (SR) paracetamol 1000 mg tablets for 12-hour drug release, integrating immediate release (IR) and controlled release (CR) layers. IR layers (300 mg paracetamol) were formulated using banana starch (BS), polyvinyl alcohol (PVA), and hydroxypropyl methylcellulose (HPMC) as release rate retardants. Selected IR and CR layers were combined into 15 SR tablet formulations (SR1-SR15) prepared by direct compression. Evaluation of post-compression parameters and *in vitro* dissolution in pH 6.8 phosphate buffer showed ten formulations achieved over 90% drug release by 12 hours. Notably, SR1 and SR3, incorporating BS in both IR and CR layers, achieved 97.12% and 95.56% release, respectively. BS demonstrated superior functionality as a disintegrating agent and rate release retardant, with direct compression providing optimal SR tablet performance for sustained therapeutic efficacy.

Keywords: *Sustained release (SR) paracetamol tablets, Immediate release (IR) and Controlled release (CR) layers, Banana starch (BS), Direct compression, In vitro evaluation parameters.*

1. INTRODUCTION

Infections such as COVID-19, dengue, malaria, and filariasis often cause high and persistent fevers that require prompt and effective treatment. With the ongoing global impact of COVID-19, managing high fever is particularly critical[1,2]. Typically, high fevers are managed with multiple doses of paracetamol, with patients commonly taking six 500 mg tablets or four 650 mg tablets daily. This results in a total daily intake of approximately 3000 mg of paracetamol, raising concerns about potential toxicity due to excessive dosage. To mitigate these risks, we aimed to develop SR paracetamol tablets containing 1000 mg of the drug, composed of a 300 mg IR layer and a 700 mg CR layer, to be taken twice daily[3,4]. For development of SR tablets preliminary works were already carried out, in these studies paracetamol 300 mg IR layers were developed with the help of BS, SSG and SSG as disintegrating agents. Direct compression and wet granulation methods were employed to prepare IR layers. As well CR layers were also developed with the use of BS, PVA and HPMC, the CR layers were also prepared as such IR layers by direct compression ad wet granulation method. All the IR and CR layers were evaluated by *in vitro* tests, and based on *in vitro* dissolution profile three IR layers and five IR layers were selected to develop a best paracetamol 100 mg SR tablet. Here, in this article we have included the development of paracetamol SR tablets with possible combinations of IR & SR layers, and selection of best paracetamol 1000 mg SR tablet with the help of in vitro evaluation parameters, probably by considering *in vitro* dissolution test. Moreover, formulations consists of BS as disintegrating agent and release rate retardant were showing best results. The disintegration and retardation of drug release from tablets due to presence of amylose and amylopectin in BS, these two absorbs water, and in disintegration due to difference in hydro static pressure to the tablet and surrounding body fluid may splits the tablet, and in rate release retardation by absorbing the water may forms dense swollen gel layer that forms a layer around the tablet obstruct or slowdowns release of drug from the tablet formulation[5,6].

2. MATERIALS & METHODS

2.1 Materials

Paracetamol, banana starch (BS), polyvinyl alcohol (PVA), Sodium Starch Glycolate (SSG), Croscarmellose Sodium (CCS), Microcrystalline Cellulose (MCC), Magnesium Stearate and Talc. All materials obtained from SK Health Care Pharma Limited, Bolaram, Hyderabad.

2.2 Methods

UV analytical method

A linearity curve for paracetamol in phosphate buffer (pH 6.8) was established to confirm system suitability for its analysis in various dosage forms using a UV-Visible Spectro photometer (Lab India, Double Beam). The process also involved identifying the drug by determining its λ_{max}. To prepare the linearity curve, a 1000 µg/ml solution was made by placing ten milli grams paracetamol in ten ml of phosphate buffer and dissolved by sonication for five minutes. From this, a 100 µg/ml solution was prepared from above stock solution by diluting one ml of above stock solution to ten ml. Further dilutions were obtained from 2 µg/ml to 16 µg/ml concentrations by drawing specific volumes (0.2 ml to 1.6 ml) of above solution (100 µg/ml), and diluting to ten ml with buffer. The λ_{max} of paracetamol was determined using either 8 or 10 µg/ml concentration, and absorbance readings were recorded for all solutions[7,8]. A linearity plot was constructed with concentration (on X-axis) versus absorbance (on Y-axis), and system suitability was validated by calculating correlation coefficient (R^2), as depicted in Figure1 and results are shown in Table 4.

Formulation of paracetamol 1000 mg SR tablets

Based on preliminary studies, 24 formulations were developed, incorporating both IR and CR layers. Among these, 12 are prepared trough direct compression, and 12 by wet granulation. The IR layer, containing 300 mg of paracetamol, utilized MCC/lactose as diluents and employed BS, SSG, and CCS as disintegrants. Magnesium stearate (Mg. stearate) and talc as lubricant and glidant, respectively. The IR formulation (IR1 to IR12) were prepared by direct compression, using disintegrants (BS, SSG, & CCS) at concentrations of 2, 4, 6 and 8% w/w per tablet. Similarly, IR13 to IR24 layers were prepared by wet granulation with same disintegrating agents and concentrations, and the total weight of IR layer was 400 mg. For the CR layers, 700 mg paracetamol was used with BS, PVA and HPMC as release rate retardants. MCC/lactose was the diluent, and the other excipients mirrored those in the IR layers. CR layers were designed with the same polymer concentrations (2%, 4%, 6% and 8% w/w per table) for both direct compression (CR1 to CR12) and wet granulation (CR13 to CR24), and the total weight of CR layer was deigned to 1000 mg. After *in vitro* testing, IR4, IR8 and IR12 were identified as the best IR formulations, while CR2, CR7, CR12, CR14, and CR23 were selected as the best CR layers. Using these, 15 SR paracetamol tablets were formulated for optimal fever management, ensuring efficacy and safety. The design for SR formulation for paracetamol were shown in Table 1, ingredients and their quantities were followed as shown in Tables 2 & 3. And the design of SR tablets was as follows- S6, S7, S8, SR9 and S10 tablets were designed with the help of IR8 layer, and combination with CR layers-CR2, CR7, CR12, CR14 and CR23. S11, S12, S13, S14 and S15 tablets were designed with the help of IR12 layer, and combination with CR layers-CR2, CR7, CR12, CR14 and CR23.

Table 1: Paracetamol 1000 mg SR Tablets design

Code for SR Tablet	Combination of CR and IR Layers
S1	IR4 + CR2
S2	IR4 + CR7
S3	IR4 + CR12
S4	IR4 + CR14
S5	IR4 + CR23
S6	IR8 + CR2
S7	IR8 + CR7
S8	IR8+ CR12
S9	IR8 + CR14
S10	IR8 + CR23
S11	IR12 + CR2
S12	IR12 + CR7
S13	IR12 + CR12
S14	IR12 + CR14
S15	IR12 + CR23

Table 2: Formulation table for Paracetamol 1000 mg SR Tablets by Direct compression CR Layers

Ingredient	S1	S2	S6	S7	S8	S11	S12	S13
Paracetamol	300	300	300	300	300	300	300	300
Banana Starch	32	32	-	-	-	-	-	-

SSG	-	-	32	32	32	-	-	-
CCS	-	-	-	-	-	32	32	32
MCC	60	60	60	60	60	60	60	60
Mg. Stearate	4	4	4	4	4	4	4	4
Talc	4	4	4	4	4	4	4	4
Paracetamol	700	700	700	700	700	700	700	700
Banana Starch	150	-	150	-	-	150	-	-
PVA	-	200	-	200	-	-	200	-
HPMC	-	-	-	-	250	-	-	250
Microcrystalline Cellulose	130	80	130	80	30	130	80	30
Mg. Stearate	10	10	10	10	10	10	10	10
Talc	10	10	10	10	10	10	10	10
Total weight	1400	1400	1400	1400	1400	1400	1400	1400

Table 3: Formulation table for Paracetamol 1000 mg SR Tablets by wet granulation method CR Layers

Ingredient	S4	S5	S9	S10	S14	S15
IR Layer						
Paracetamol	300	300	300	300	300	300
BS	32	32	-	-	-	-
SSG	-	-	32	32	-	-
CCS	-	-	-	-	32	32
MCC	60	60	60	60	60	60
Mg. Stearate	4	4	4	4	4	4
Talc	4	4	4	4	4	4
CR Layer						
Intragranular						
Paracetamol	700	700	700	700	700	700
BS	150	-	150	-	150	-
PVA	-	-	-	-	-	-
HPMC	-	200	-	200	-	200
Lactose	30	30	30	30	30	30
Extragranular						
Lactose	100	50	100	50	100	50
Mg. Stearate	10	10	10	10	10	10
Talc	10	10	10	10	10	10
Total Weight	1400	1400	1400	1400	1400	1400

Table 2 describes about design of paracetamol 1000 mg SR tablets consists of CR layers prepared direct compression method, and Table 3 describes about design of paracetamol 1000 mg SR tablets consists of CR layers prepared wet granulation method, the total weight of SR tablet was 1400 mg. The procedure for preparation of paracetamol 1000 mg SR tablets were as follows- initially CR layer was compressed, and on same layer the IR layer was placed and compressed as double layer tablet by maintaining tablet hardness between 6 to 7 kg/cm^2 using 16-station Cadmach punching machine with the use of using 16 mm x 9 mm oblong punches[9,10], then all the paracetamol SR formulations were evaluated by post compression parameters.

2.3 Evaluation of paracetamol 1000 mg SR Tablets

Post-compression evaluation parameters

Weight variation

Individual weights of randomly selected 20 tablets are recorded to determine the mean weight. Weight variation was calculated using the mean and individual weights with as follows,

Weight variation (%) = { [(Individual mass-Mean mass) /Mean mass] x 100}

Limits for acceptance criteria was ±5% for weight variation of these paracetamol SR tablets, because of their individual tablet weight is more than 250 mg[11,12].

Hardness Test

The hardness of five randomly selected paracetamol SR tablets of each batch was tested using a hardness tester (Monsanto), with an acceptance criteria of ± 5% for each batch[13,14].

Friability Test

Tablet number equal to 6.25 g were picked randomly from each batch of paracetamol SR tablets, weight was measured and considered as initial weight, W_1. 10 tablets are placed in friability apparatus (Kshitij), operated at 25 rpm for four minutes, and then removed for assessment. Each tablets was cleaned with a soft cloth and weight of all ten tablets were measures, and was considered as final weight, W_2. % friability was calculated by considering W1 & W2 values by using following formula

% Friability =\{ [$(W_1-W_2)/(W_1)$] x 100\}

The acceptance criteria for all SR tablets was % friability should be <1% for all paracetamol SR tablets[15,16].

In vitro dissolution evaluation

A total of six tablets from each batch were randomly chosen and placed in 900 ml of phosphare buffer (pH 6.8) at 37±0.5°C, with stirring at 50 rpm using paddle apparatus. (USP Apparatus II). At predetermined time points as shown at Table 7, five ml samples were withdrawn and replaced with equal volume of fresh buffer.All the samples are diluted preporely and evaluated using Lab India Double Beam UV-Spectro Photo meter at 245 nm to know the Cumulative % Drug Release using following formula[17,18], with the use of absorbance of test(A_T), absorbance of standard (A_S), dilution of test (D_T) and dilution of standard (D_S).

Cumulative % Drug Released = [(A_T/A_S) x (D_S/D_T) x 100]

Assay

20 tablets were picked from each batch of SR tablets and grounded finely in a mortar and, one tablet weight of powder was picked from mortar, placed and sonicated to dissolve in phosphate buffer (pH 6.8). Then samples are diluted preporely, and evaluated using Lab India Double Beam UV-Spectro Photo meter at 245 nm and evaluated % assay using follow equitation[19,20] with the use of absorbance of test(A_T), absorbance of standard (A_S), dilution of test (D_T) and dilution of standard (D_S).

% Assay = [(A_T/A_S) x (D_S/D_T)]

The acceptance criteria for % assay is 90% to 110%.

3. RESULTS & DISCUSSION

3.1 UV analytical method

Table 4: Standard calibration graph for paracetamol in pH 6.8 phosphate buffer

Concentration (µg/ml)	Absorbance
2	0.113 ± 0.01
4	0.226 ± 0.02
6	0.339 ± 0.02
8	0.452 ± 0.03
10	0.565 ± 0.04
12	0.678 ± 0.04
14	0.791 ± 0.03
16	0.904 ± 0.03

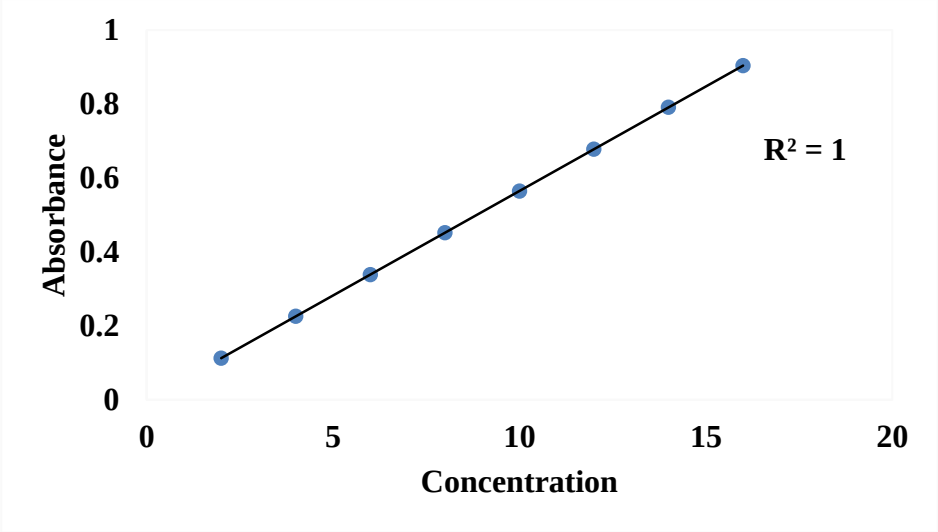

Figure 1: Standard calibration graph for paracetamol in pH 6.8 phosphate buffer

The observed λ_{max} for paracetamol in pH 6.8 phosphate buffer was 245 nm, which was the same standard value for paracetamol in pH 6.8 phosphate buffer i.e. 245 nm. Hence it was identified and confirmed that the drug analyzed by the UV-Spectro photo meter was Paracetamol.

From the above Table 4 & Figure 1, it was observed that the R^2 value for calibration curve of paracetamol in pH 6.8 phosphate buffer was observed to be 0.999 at concentration range between 2 to 16 µg/ml, measured at 245 nm. Hence, it was confirmed that these concentration ranges producing linearity in estimation and obeying Beer-Lambert's law, and UV-Spectro photo meter was accurate and could be able to analyse paracetamol in various formulations.

3.2 Post-compression evaluation

Table 6: Post-compression evaluation for S1 to S15

Formulation Code	Thickness (mm)	Weight Variation (%)	Hardness (kg/cm²)	Friability (%)	Assay (%)
S1	5.52 ± 0.42	2.95 ± 0.21	6.5 ± 0.52	0.32 ± 0.01	98.76 ± 5.92
S2	5.55 ± 0.40	3.12 ± 0.24	6.3 ± 0.54	0.38 ± 0.02	99.12 ± 6.34
S3	5.48 ± 0.38	3.05 ± 0.26	6.7 ± 0.38	0.40 ± 0.03	98.83 ± 7.24
S4	5.60 ± 0.44	3.10 ± 0.23	6.7 ± 0.37	0.41 ± 0.01	98.85 ± 6.95
S5	5.50 ± 0.48	2.95 ± 0.19	6.8 ± 0.42	0.36 ± 0.02	99.25 ± 7.82
S6	5.53 ± 0.43	2.88 ± 0.15	6.6 ± 0.46	0.34 ± 0.02	99.45 ± 8.05
S7	5.57 ± 0.51	3.20 ± 0.22	6.8 ± 0.51	0.36 ± 0.01	99.29 ± 7.28
S8	5.49 ± 0.49	2.96 ± 0.20	6.4 ± 0.53	0.39 ± 0.02	98.94 ± 6.98
S9	5.58 ± 0.47	3.18 ± 0.26	6.6 ± 0.38	0.43 ± 0.03	99.03 ± 7.54

S10	5.51 ± 0.37	3.22 ± 0.30	6.5 ± 0.41	0.38 ± 0.03	99.34 ± 8.88
S11	5.53 ± 0.34	3.02 ± 0.29	6.5 ± 0.53	0.33 ± 0.01	99.38 ± 8.08
S12	5.59 ± 0.38	3.14 ± 0.25	6.9 ± 0.49	0.35 ± 0.01	99.65 ± 6.82
S13	5.54 ± 0.37	3.07 ± 0.20	6.6 ± 0.41	0.37 ± 0.01	99.01 ± 7.56
S14	5.55 ± 0.42	3.05 ± 0.28	6.9 ± 0.38	0.39 ± 0.02	98.92 ± 8.01
S15	5.56 ± 0.0	2.98 ± 0.22	6.7 ± 0.44	0.35 ± 0.02	99.18 ± 6.76

The following post-compression values were found for all the paracetamol SR tablets for S1 to S24 from the Table 6 and were as follows- the weight variation values were in between 1.93 to 4.24%, hardness values were in between 6.1 to 7.1 kg/cm^2, friability values were in between 0.10 to 0.73%, and assay values were in between 98.29 to 99.86%. The observations from post-compression parameters of all tablet formulations from SR1 to SR24 inferences that, all the formulations weight variation was with in the acceptance limits indicates that uniformity in tablet weight. Hardness values indicates that tablets had good mechanical strength and tablets may possess good physical stability to with stand various mechanical agitations that tablet experience while packing, shipping and etc. The friability values indicates tablets may with stand to breakage while handling. And the assay values were assured uniformity of dose foe all formulations from S1 to S24.

***In vitro* dissolution Data**

Table 7: *In vitro* dissolution data for paracetamol 1000 mg SR tablets (S1-S15)

Time (hour)	Cumulative % Drug Released														
	S1	S2	S3	S4	S5	S6	S7	S8	S9	S10	S11	S12	S13	S14	S15
0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
008	6.28	6.36	6.17	6.41	6.52	7.51	7.59	7.62	7.67	7.73	8.07	8.41	8.47	8.51	8.67
0.16	10.48	10.50	10.68	10.72	10.84	12.34	12.47	12.53	12.60	12.64	12.68	12.64	12.68	12.72	12.83
0.25	15.72	15.80	15.91	15.87	15.90	16.28	16.34	16.50	16.55	16.58	17.17	17.26	17.45	17.56	17.42
0.33	19.24	19.37	19.48	19.54	19.67	21.38	21.42	21.57	21.61	21.70	21.64	21.45	21.63	21.70	21.68
0.41	24.52	24.60	24.10	24.41	24.50	25.45	25.50	25.67	25.79	25.31	25.51	25.60	25.61	25.68	25.47
0.5	31.91	31.83	31.94	30.49	28.39	30.12	30.19	30.46	30.54	30.67	29.47	29.51	29.77	29.58	29.89
1	35.73	34.21	36.28	34.36	31.78	32.23	32.31	32.40	32.47	32.52	32.81	32.48	32.50	32.61	32.56
1.5	38.50	37.89	39.90	36.71	34.91	36.45	37.27	37.49	35.60	36.71	36.27	37.81	37.93	35.44	36.47
2	41.29	41.26	42.37	39.43	36.50	39.36	39.45	40.51	38.98	38.40	39.36	39.42	40.15	38.61	38.59
3	46.1	46.3	46.4	44.5	39.6	42.6	42.7	44.0	41.5	40.6	42.1	42.7	44.0	41.0	40.1

	2	9	2	7	5	1	2	9	7	4	2	8	1	2	2
4	52.47	51.83	51.94	49.65	45.72	48.37	48.52	47.13	46.18	46.51	48.33	48.47	47.26	46.58	46.28
5	57.31	56.47	56.51	54.28	50.35	53.24	53.34	53.64	51.13	52.17	53.78	53.81	53.54	51.23	52.47
6	63.59	61.71	62.84	59.91	56.85	58.01	59.11	58.27	55.34	58.72	58.47	59.43	58.92	55.89	58.23
7	69.47	66.34	67.41	64.28	62.34	62.14	65.43	63.70	60.11	63.25	62.91	65.66	63.42	60.47	63.45
8	74.23	71.27	73.32	69.61	67.29	67.28	70.24	69.37	65.81	69.90	67.88	70.48	69.60	65.47	69.78
9	80.96	76.31	78.45	74.57	73.12	72.49	76.61	74.06	70.46	74.53	72.72	76.47	74.57	70.89	74.52
10	85.25	81.64	84.70	78.87	78.98	77.19	81.22	80.40	75.18	80.79	77.12	81.61	80.41	75.58	80.41
11	91.75	85.76	90.81	83.56	84.57	82.76	87.90	86.97	80.43	86.01	82.45	87.33	86.62	80.91	86.10
12	97.12	90.42	95.56	88.39	90.05	87.45	93.47	91.59	85.13	91.13	87.81	93.47	91.81	85.23	91.14

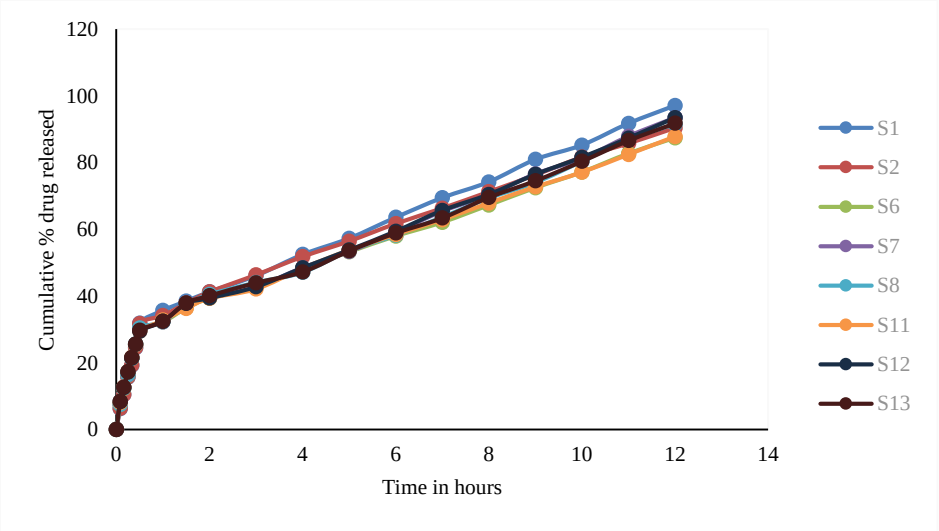

Figure 2: *In vitro* dissolution data for paracetamol 1000 mg SR tablets prepared by direct compression method

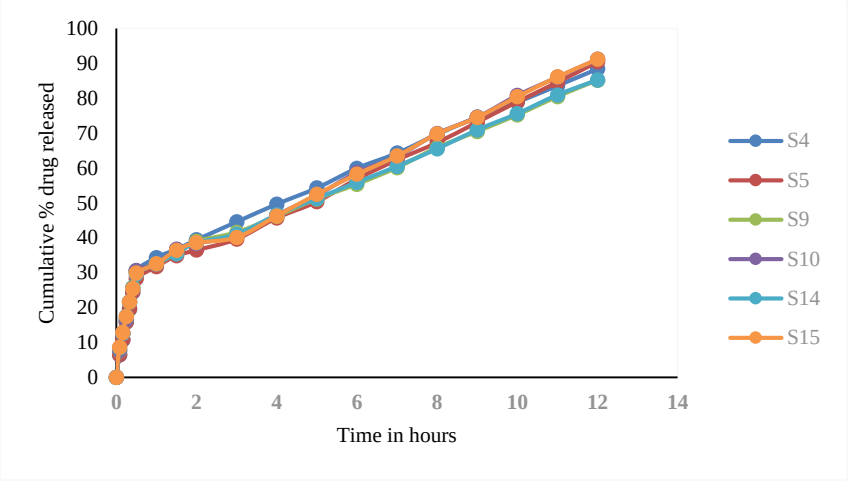

Figure 3: *In vitro* dissolution data for paracetamol 1000 mg SR tablets prepared by wet granulation method

A two-way ANOVA was conducted to assess the effect of time and formulation on the *in vitro* dissolution of drug release (Table 7). The analysis revealed a statistically significant main effect of time ($F(14,210) = 1342.28$, $p < 0.0001$), indicating that cumulative drug release significantly increased over time across all formulations. The formulation factor also exhibited a significant impact on drug release ($F(14,210) = 415.73$, $p < 0.0001$), suggesting that different formulations influenced the dissolution profile. Additionally, a statistically significant interaction effect between time and formulation ($F(196,210) = 6.21$, $p < 0.0001$) was observed, confirming that the dissolution behavior varied for each formulation over time.

Table 7 and Figure 2 & 3 describes about the SR tablet prepared by IR4 layer combinations, where all formulations have shown good extension of release up to 12th hour. The ascending order for *in vitro* drug release of these paracetamol 1000 mg SR tablets were as follows,

S4 (Approx. 88%) < S5 (Approx. 90%) < S2 (Approx. 90%) < S3 (Approx. 96%) < S1 (Approx. 97%).

Table 7 and Figure 2 & 3 describes about the SR tablet prepared by IR8 layer combinations, where all formulations have shown good extension of release up to 12th hour. The ascending order for *in vitro* drug release of these paracetamol 1000 mg SR tablets were as follows,

S9 (Approx. 85%) < S6 (Approx. 87%) < S210 (Approx. 91%) < S3 (Approx. 92%) < S1 (Approx. 93%)

Table 7 and Figure 2 & 3 describes about the SR tablet prepared by IR12 layer combinations, where all formulations have shown good extension of release up to 12th hour. The ascending order for *in vitro* drug release of these paracetamol 1000 mg SR tablets were as follows,

S14 (Approx. 85%) < S11 (Approx. 88%) < S15 (Approx. 91%) < S13 (Approx. 92%) < S1 (Approx. 93%)

Finally, from *in vitro* dissolution data of paracetamol 1000 mg SR tablets it was inference that, all the formulations were extending paracetamol up to 12th hour, but, only ten out of 15 SR tablets were releasing more than 90% of drug from them. Among ten SR tablets, only two SR tablets only were releasing more than 95% of drug, and they are S1 and S3. S1 was releasing 97.12% and S3 was releasing 95.56% *in vitro* drug release at 12th hour. S1 designed by IR4 layer and CR2 layer, where both the layers were prepared with the help of direct compression method. And, S3 was designed of IR4 and CR12 layers, these two layer were also prepared by direct compression method. Where, S1 & S3 tablet were designed with BS as disintegrating agent in IR layer and as Rate release retardant in CR layer.

***In vitro* Drug Release Kinetics**

Table 8: *In vitro* Drug Release Kinetic profile for tablet formulations S1 to S15

Formulation Code	Zero-order (R^2)	First-order (R^2)	Higuchi (n)	Korsmeyer-Peppas (n)
S1	0.931 ± 0.06	0.704 ± 0.05	0.983 ± 0.07	0.957 ± 0.08
S2	0.917 ± 0.04	0.691 ± 0.02	0.982 ± 0.07	0.954 ± 0.08
S3	0.924 ± 0.04	0.693 ± 0.01	0.980 ± 0.05	0.953 ± 0.05

S4	0.920 ± 0.03	0.699 ± 0.02	0.982 ± 0.04	0.955 ± 0.07
S5	0.942 ± 0.04	0.738 ± 0.05	0.976 ± 0.05	0.956 ± 0.06
S6	0.924 ± 0.05	0.730 ± 0.06	0.980 ± 0.07	0.960 ± 0.04
S7	0.939 ± 0.06	0.749 ± 0.04	0.979 ± 0.05	0.963 ± 0.08
S8	0.932 ± 0.04	0.739 ± 0.04	0.977 ± 0.04	0.961 ± 0.07
S9	0.921 ± 0.06	0.730 ± 0.01	0.975 ± 0.06	0.955 ± 0.07
S10	0.938 ± 0.03	0.753 ± 0.03	0.976 ± 0.07	0.959 ± 0.06
S11	0.927 ± 0.05	0.744 ± 0.05	0.982 ± 0.07	0.967 ± 0.02
S12	0.940 ± 0.06	0.765 ± 0.05	0.980 ± 0.05	0.970 ± 0.05
S13	0.934 ± 0.05	0.758 ± 0.03	0.979 ± 0.06	0.968 ± 0.03
S14	0.926 ± 0.07	0.752 ± 0.02	0.977 ± 0.04	0.964 ± 0.05
S15	0.941 ± 0.06	0.774 ± 0.04	0.976 ± 0.05	0.966 ± 0.06

Table 8 reveals that the correlation coefficient (R^2) values for the zero-order plots ranged from 0.917 to 0.945, while the values for the first-order plots were between 0.61 and 0.774. Similarly, correlation coefficient (n) value for Higuchi plots ranged from 0.975 to 0.983, and then n-value for the Korsmeyer-Peppas plots were observed to be between 0.953 to 0.970.

From *in vitro* pharmacokinetic data, it was inference that the order of paracetamol release from all SR tablets were dominating by zero-order, the mechanism of paracetamol release from SR tablets is following diffusion and especially non-Fickian diffusion, anomalous transport.

4. CONCLUSIONS

UV- Visible Spectrophtometer, double beam is suitable to analyse paracetamol in various formulations that are used to analyse by it, because paracetamol in pH 6.8 phosphate buffer at concentration range 2-16 µg/ml was obeying Beer-Lambert's law by showing linearity (R^2 value = 0.999), as shown in Figure 1. And the drug used was identified as paracetamol because it was showing λ_{max} = 245 nm in pH 6.8 phosphate buffer, when analyzed by of UV-Visible Spectrophto meter, double beam. Paracetamol Paracetamol SR layers are having good mechanical strength to handle them feasibly, this was came to know from various post-compression parameters as shown in Table 6. Paracetamol 1000 mg SR tablets prepared by the use of BS as disintegrating agent in IR layer, and as a rate release retardant (polymer) in CR layer were showing highest *in vitro* paracetamol release compared to other disintegrating agents and release rate retardants used. IR and CR layers tableted by direct compression, and tablets prepared by direct compression are suitable to design SR tablets. Because they are showing highest *in vitro* paracetamol release compared to wet granulation method. Finally, SR1 was considered as final selected best formulation, that is having 97%(approximately 100%) *in-vitro* paracetamol release at the end of 12th hour. S1 is designed by BS as disintegrating agent at 8% w/w per tablet weight in IR layer and as rate release retardant (polymer) at 25% w/w per tablet weight in CR layer. S1 follows a zero-order release profile, with drug release occurring via a non-Fickian diffusion mechanism, specifically anomalous transport. Mechanism of disintegration of IR layer is because of absorption of water that increases hydrodynamic pressure inside the tablet due to the swollen BS layer, this may leads to differ in hydrodynamic pressure with surrounding gastro-intestinal fluid leads to disintegration. And the controlled release is due to absorption of water may forms dense viscous swollen gel of banana starch around the CR layer will slowdown the release and control the release of paracetamol from CR layer .

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