WWW.IJRPR.COM

International Journal of Research Publication and Reviews

Journal homepage: www.ijrpr.com ISSN 2582-7421

Enhanced Sustained Release Profile of Paracetamol Matrix Tablets Achieved through Direct Compression of Hydrophilic Polymer Systems

Harshit Gupta[a], Esha Agarwal [a], Shweta Raghav [a], Sourav [a], Teetu Kumar [a], Abdul Ahad Noor [a], Vikrant [a], Gulshan Rathore[b*]

[a]M.Pharm Scholar, Department of Pharmaceutics, Teerthanker Mahaveer College of Pharmacy,Teerthanker Mahaveer University, Moradabad-244001, India

[b]Assistant Professor, Department of Pharmaceutics, Teerthanker Mahaveer College of Pharmacy,Teerthanker Mahaveer University, Moradabad-244001, India

A B S T R A C T :

Despite being widely used, the oral route frequently leads to poor absorption for many medications, such as paracetamol, which must be taken frequently (every 4-6 hours) due to its short half-life. This study fills a gap in the literature by creating a sustained-release PCM matrix tablet and using the Direct Compression method, which is the most straightforward and cost-effective manufacturing technique, to avoid the problems of wet granulation. The goal was to develop a formulation that would increase patient adherence by prolonging the medication's release for 8–12 hours. Five formulations(F1-F5) were made using varying concentrations of the synthetic polymer hydroxypropyl methylcellulose (HPMC). The pre-compression mixture's good flow characteristics were shown by positive values for the angle of repose, bulk density, tapped density, and Carr's index. Each compressed tablet met quality standards for hardness (4.2–5.4 kg/cm2), weight fluctuation, and friability, demonstrating exceptional physical attributes. In vitro dissolution experiments lasting up to 10 hours showed an inverse relationship between the drug release rate and the HPMC content. Formulation F5, which had the highest HPMC concentration, produced the most desirable sustained-release profile. This proved that a therapeutically and industrially scalable SR paracetamol matrix tablet could be successfully created using the polymer combination and direct compression method.

Keywords: Direct Compression, Hydrophilic Polymer, Matrix Tablets, Release kinetics, Sustained-Release

1. Introduction

Oral route is one of the most common methods for delivering drugs. It is easy to use, patients stick to it well, it has low sterility needs, and it offers flexible dosage forms. Today, over 90% of the formulations made are taken orally. When given in a standard dosage form, many oral medications show poor bioavailability. This means their absorption rate and extent are lower than ideal. PCM, or paracetamol, comes in standard dosage forms. Due to the limitations of the GI tract, the drug's bioavailability from a standard dosage form is 60%. Since frequent dosage is required due to the drug's rapid absorption but short half-life, patients find it difficult to maintain effective plasma levels. A sustained-release drug delivery system, also known as zero order dissolution, is designed to deliver medication to the body at a predetermined pace. This prolonged, consistent release maximizes the duration of the drug's absorption window in the GI tract and is a crucial strategy for improving the degree and consistency of the drug's overall bioavailability. This helps to maintain a constant drug level, usually for a long period of time.[1]

Comparing sustained release delivery systems to instant release forms shows several benefits. These include reducing the number of doses to once or twice daily, improving patient adherence, and minimizing gastrointestinal side effects due to less fluctuation in plasma drug levels. Steady drug release lowers the total amount of medication needed and results in a more consistent drug effect.[2,3,4] The simplicity, durability, and flexibility of matrix tablets make them one of the most researched ways to deliver drugs over a long period. The medication is evenly spread within a polymer matrix, which controls its release through processes like erosion, swelling, and diffusion. Hydrophilic polymers, such as carboxymethyl cellulose, sodium alginate, xanthan gum, and hydroxypropyl methylcellulose (HPMC), absorb water and swell, creating a gel barrier that slows down drug diffusion.[5]

On the other hand, hydrophobic polymers like waxes, polyvinyl acetate, or ethylcellulose stop water from getting in and offer diffusion-controlled release through matrix pores. Research shows that using both hydrophilic and hydrophobic polymers results in better control over drug release. This combination allows for repeatable and predictable sustained-release profiles.[6] Paracetamol (acetaminophen) is one of the most common pain relievers and fever reducers. It is a good option for sustained release formulation. It has a short elimination half-life of two to three hours because of its high water solubility and fast absorption from the digestive system. As a result, traditional immediate-release formulations often require frequent doses to maintain therapeutic plasma levels, typically every 4 to 6 hours.[7] In chronic illnesses like osteoarthritis, back pain, or a persistent fever, frequent dosing may lower patient compliance. A prolonged-release matrix tablet that contains paracetamol can extend the drug's release for 8 to 12 hours. This reduces how often patients need to take the medicine, maintains steady therapeutic levels, and improves patient compliance.[8] Paracetamol matrix systems also have the benefit of minimising plasma concentration swings, which lowers the possibility of adverse effects including hepatotoxicity linked to elevated plasma levels. In this

way, a well-designed sustained release matrix composition meets the demands of the patient as well as the clinician Of the tablet manufacturing processes—which include melt extrusion, wet granulation, dry granulation, and direct compression—direct compression is the most straightforward and economically feasible. .[9] By mixing and compressing the drug and excipients into tablets, direct compression does away with the need for granulation or drying. As a result, less specialised equipment is needed, less time is spent processing, and less money is spent manufacturing.[10]

Paracetamol has special advantages when compressed directly. When using traditional granulation techniques, paracetamol often presents formulation issues because it is a heat-stable but poorly compressible medication. When combined with the appropriate excipients and polymers, direct compression offers adequate compressibility and hardness while guaranteeing consistent drug release. Furthermore, since no solvents or water are used, paracetamol's stability remains unaffected.[11] In spite of its heat stability, paracetamol is considered a poorly compressible drug when taken on its own, often necessitating the use of complex, multi-step granulation processes. Direct Compression is the better choice because it circumvents this limitation by using particular excipients and high-compressibility polymers (like HPMC and CMC).[12] When properly mixed, these ingredients form a cohesive, free-flowing powder that ensures adequate tablet hardness and strength without the need for heat or water while maintaining content homogeneity.

Direct compression is also perfect for large-scale industrial manufacturing because it operates with high-speed tablet presses. Direct compression is ideally suited to the pharmaceutical industry's transition to continuous manufacturing because it reduces complexity and ensures consistency. It also meets regulatory standards for cost-effectiveness, reproducibility, and quality by design (QbD).[13] For paracetamol sustained release formulations, direct compression streamlines, speeds up, and reduces the cost of the formulation process while maintaining the desired drug release characteristics, in contrast to wet granulation.[14] Extended-release paracetamol formulations have been the subject of numerous studies. However, the majority of these experiments have relied on wet granulation techniques due to the poor flowability and compressibility of paracetamol. Wet granulation improves content consistency and mechanical strength, but it is expensive, time-consuming, and unsuitable for moisture-sensitive compositions.[15]

This leads to a significant gap in the literature: there aren't many studies on direct compression-based paracetamol sustained release matrix tablets that employ novel natural and synthetic polymer combinations. This gap suggests an opportunity to research and enhance such formulations for both therapeutic efficacy and industrial viability.[16] The current study intends to develop prolonged release matrix tablets of paracetamol by the direct compression method, utilizing a blend of natural and synthetic polymers for optimal release. The research aims to develop a formulation that prolongs drug release for up to 8–12 hours, reduces dose frequency, and improves patient adherence.[17]

2. Materials and Methods

2.1 Materials

Paracetamol, HPMC (Hydroxy Propyl Methyl Cellulose) [3000cPs], CMC (Carboxymethyl Cellulose) [1100-1900cPs], Talc, Magnesium Stearate, Sodium Starch Glycolate, Dibasic calcium phosphate dihydrate (DCPD) were provided by departmental chemical store of Teerthanker Mahaveer College of Pharmacy.

2.2 Methods

2.2.1 Pre-compression Parameters

Angle of repose

The angle of repose was determined using the fixed funnel method. A funnel was kept vertically in a stand at a specific height above a piece of paper that was spread out on a horizontal surface. The funnel was closed and a granule was added. The funnel was then opened, releasing the grains onto the paper in a smooth, conical pile. After determining the height and radius of the heap, the angle of repose was calculated using the following formula. [18,19]

$Ø = \tan^{-1} h/r$

Where Ø = Angle of repose, h =height of heap and r = radius

Bulk Density

The bulk volume was measured after a predetermined amount of granules were carefully levelled without compacting them in a 25 ml measuring cylinder. The bulk density was computed using the formula.[20]

Bulk density = Weight of granules/ bulk volume

Tapped Density

The tapped density was measured using digital bulk density equipment. The measuring cylinder was filled with a predetermined number of granules, tapped 100 times, and the tapped volume was noted. The tapped density was computed using the formula.[20]

Tapped Density = Weight of granules / tapped volume

Compressibility Index

The compressibility index (CI), also known as Carr's Index, measures a powder's flowability by indicating its capacity to reduce volume under pressure.

It is calculated using the bulk and tapped densities of a powder; lower compressibility index values indicate better flow characteristics.[21]
Compressibility Index= [Tapped density- Bulk density/Tapped density] ×100

Hausner's Ratio

Hausner's Ratio was determined by following formula:

Hausner's Ratio= Tapped density / Bulk density

2.2.2 Preparation of calibration curve

Exactly 100 milligrams of paracetamol were used in a 100 microgram per ml volumetric flask. Enough buffer solution was added to the mark (stock solution) to fill it. The standard solution, which was divided into two micro gram per ml, four micro gram per ml, six micro gram per ml, eight micro gram per ml, and ten micro gram per ml, was used to fill ten micro gram per ml of the capacity with phosphate buffer of pH 7.2. The absorbance of these solutions was measured at a suitable wavelength using spectrophotometry.[22] The observed absorbance was plotted against the concentration in the graph given below:

2.3 Fabrication of Sustained Release Matrix Tablets by Direct Compression

All the drugs and excipients were passed through sieve number 40 or 60. Accurately weigh drug and excipients were thoroughly mixed usually with V-Cone blender. Glidant and lubricant were finally added to the blend and mixed. The produced mixture was compressed into tablet using Semi-automatic Punching machine. Table 1 show the composition of prepared paracetamol sustained release matrix tablet.[23]

Table 1. Formulation Table

S.No.	*Paracetamol (mg)*	*HPMC*	*DCPD*	*CMC*	*Sodium Starch Glycolate*	*Talc*	*Magnesium Stearate*
F1	40	30	70	38	16	4	2
F2	40	40	70	38	16	4	2
F3	40	50	70	38	16	4	2
F4	40	60	70	38	16	4	2
F5	40	70	70	38	16	4	2

2.4 Evaluation of tablet

2.4.1 Hardness

The hardness measurement procedure includes testing the tablets' crushing strength. It gives the table its breaking power, and the tablets' actual hardness shows how strong they are. The hardness was measured using a Pfizer hardness tester. It is possible to measure the hardness of ten tablets. The Value of hardness was measured in kg/cm2. Average hardness was noted. Both before and after compression, the tablets' hardness was evaluated.[24]

2.4.2 Weight variation test

To investigate weight variance, twenty tablets of each formulation were chosen at random during compression, and an electronic balance was used to calculate the average weight of each tablet. Every tablet was also weighed.[25]
Limit: Weight of individual tablet should be in the limit of average weight ±5%

2.4.3 Friability

The test was carried out using a ROCHE FRIABILATOR. Ten tablets were taken, carefully weighed, dedusted, and placed in a drum prior to testing. The tablets were removed after the drum had rotated 100 times. Removed loose dust from the tablets as before, and weighted accurately.[26]

2.4.4 In-vitro dissolution profile

The in vitro releases of paracetamol from different batches were tested for two hours in an acidic pH and eight hours in phosphate buffer using a USP-II paddle-type dissolution apparatus. Distinct release patterns were seen for different polymer concentrations. Most of the formulations released more than 80% to 90% during the 10-hour study period, based on the release data of various formulations. F5, which had a higher HPMC content than the others, showed better sustained release characteristics as more HPMC creates a thicker, stronger gel layer around the tablet, which slows the drug release down.[27]

2.4.5 Kinetics analysis of developed formulations

To understand the mechanism and rate-controlling parameters influencing the drug release from the Paracetamol matrix tablets, the dissolving data for each of the five formulations (F1–F5) was fitted to zero-order, first-order, and Higuchi kinetic models.

3. Results

3.1 Pre-compression Parameters

All of the paracetamol matrix tablets were made using the HPMC Polymer in different formulations and concentrations. The matrix tablet is primarily made using the Direct Compression Method. Every matrix tablet produced as a result has excellent quality in terms of Angle of Repose, Bulk density, Tapped Density, Compressibility index and Hausners Ratio.[Table 2]

Table.2 Precompression Parameters

Batch Code	*Evaluating parameters*				
	Angle of repose (°)	*Bulk density gm/cm^3*	*Tapped density gm/cm^3*	*Compresibility index (%)*	*Hausner ratio*
F1	32.4	0.42	0.5	16	1.19
F2	31.7	0.44	0.52	15.4	1.18
F3	30.9	0.45	0.53	15.1	1.17
F4	29.8	0.46	0.54	14.8	1.17
F5	28.6	0.47	0.55	14.5	1.16

3.2 Preparation of calibration curve

A standard calibration curve of paracetamol in phosphate buffer (7.2 pH) showed linearity in the range of 0–10 microgram/ml, with a correlation coefficient (R2) of 0.9998.

Table.3 Data for Standard curve of paracetamol in phosphate buffer of pH 7.2

S. No.	*Concentration(microgm/ml)*	*Absorbance*
1.	0	0
2.	2	0.128
3.	4	0.258
4.	6	0.386
5.	8	0.521
6.	10	0.658

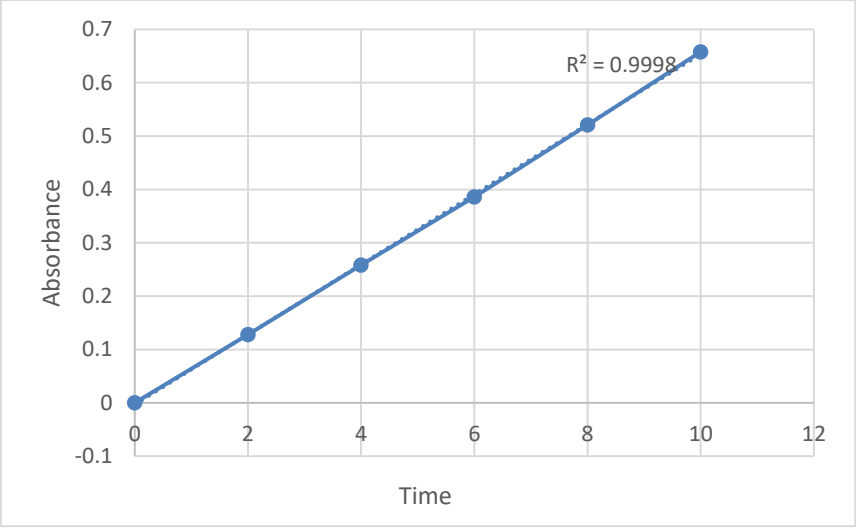

Fig. 1 – Standard Calibration Curve of Paracetamol

3.3 Evaluation of Formulated Tablets

3.3.1 Hardness

The hardness ranged from 4 to 5.5 g/cm2, according to the Monsanto type hardness tester, which was ideal for the matrix formulation requirement. [Table 4]

3.3.2 Weight variation test

The weight variation study involved 20 participants in randomly selected samples from each batch; the weight uniformity results of the manufactured matrix tablets indicate that the average weight of each tablet does not differ significantly, and the variation was found to be within the acceptable range. [Table 4]

3.3.3 Friability

The friability of all the formulations ranges between 0.55%-0.68 %, according to the Roche Friabiliter which is within the acceptable limits i.e.<1%[Table 4]

3.3.4 In Vitro-dissolution Profile & Kinetics analysis of developed formulations

The in vitro releases of paracetamol from different batches were tested for two hours in an acidic pH and eight hours in phosphate buffer using a USP-II paddle-type dissolution apparatus. Distinct release patterns were seen for different polymer concentrations. Most of the formulations released more than 80% to 90% during the 10-hour study period, based on the release data of various formulations. F5, which had a higher HPMC content than the others, showed better sustained release characteristics as more HPMC creates a thicker, stronger gel layer around the tablet, which slows the drug release down. [Table 5 & 6], [Figure 2 & 3]

Table.4 Evaluated Parameters of Formulated Tablets

Batch Code	***Evaluating parameters***				
	Hardness (kg/cm^2)	***Weight variation (%)***	***Friability (%)***	***Thickness***	***Drug Content (%)***
F1	4.2	±2.1	0.68	0.4	97.3
F2	4.5	±1.9	0.65	0.34	90.3
F3	4.8	±1.8	0.62	0.3	94.6
F4	5.1	±1.6	0.58	0.41	92.4
F5	5.4	±1.5	0.55	0.35	93.1

Table 5. Zero order and higuchi release for the following formulations

Time (Mins)	**√T**	**% Cumulative amount of drug release**				
		Formulation Code				
		F1	**F2**	**F3**	**F4**	**F5**
1	1.00	6	5	4	3	2
2	1.41	11	9	7	6	4
3	1.73	16	13	11	8	6
4	2.00	21	18	14	11	8
5	2.24	26	22	19	14	10
6	2.45	31	26	24	17	12
7	2.65	36	30	27	20	14
8	.83	41	34	30	22	16
9	3.00	46	38	33	25	18
10	3.16	50	42	36	27	20

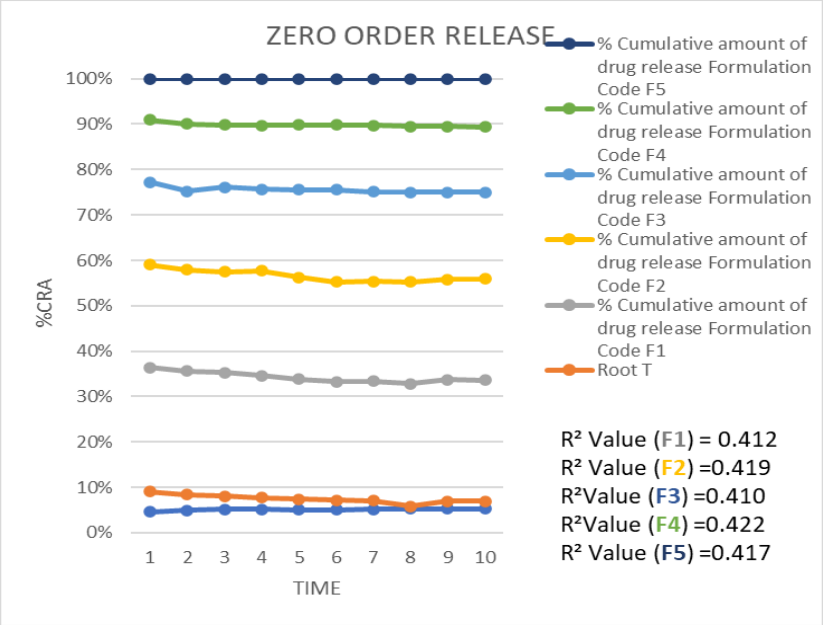

Figure.2 Zero order release

Table 6. First Order Release

Time	*%ARA*				
	F1	*F2*	*F3*	*F4*	*F5*
1	0.75	0.6	0.45	0.3	0.15
2	1.49	1.2	0.9	0.6	0.3
3	2.23	1.79	1.35	0.9	0.45
4	2.96	2.39	1.8	1.2	0.6
5	3.68	2.99	2.24	1.49	0.75
6	4.4	3.59	2.69	1.79	0.9
7	5.11	4.19	3.14	2.09	1.05
8	5.81	4.78	3.59	2.39	1.2
9	6.51	5.38	4.04	2.69	1.35
10	7.21	5.98	4.49	2.99	1.49

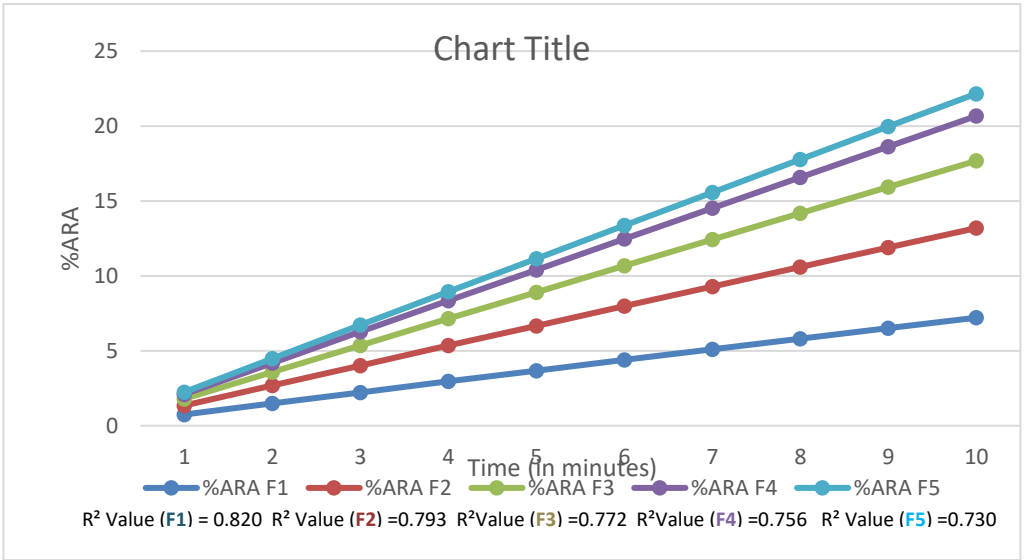

Figure.3 First order release

4. Conclusion

In this study, we employed the direct compression technique to formulate and evaluate sustained release (SR) paracetamol tablets utilizing hydrophilic polymers. The aim of the formulation was to provide an extended release of drug for 8-12 hours, to address the short half-life of the drug and frequent dosage of the drug. The pre-compression excipient properties, including angle or repose, values equals (32.4° - 28.6°), bulk density values equals (0.42 - 0.47 g/cm³), tapped density values equals (0.50 - 0.55 g/cm³) and Carr's index (16% - 14.5%) values, signified good powder flow properties. The results demonstrate the powder blend has good compressibility and homogeneity.

Acknowledgements

The Teerthanker Mahaveer College of Pharmacy (TMCOP) have our sincere gratitude for providing the essential resources and state-of-the-art facilities. We would especially like to express our gratitude to them for their invaluable advice and administrative support throughout this investigation. We thank the technical team as well.

Conflict of interest

The authors of this research article declare that they have no conflicts of interest with regard to its publication.

REFERENCES

1. Alqahtani MS, Kazi M, Alsenaidy MA, Ahmad MZ. Advances in Oral Drug Delivery. Front Pharmacol. 2021 Feb 19;12:618411. doi: 10.3389/fphar.2021.618411. PMID: 33679401; PMCID: PMC7933596.
2. Kalantzi LE, Karavas E, Koutris EX, and Bikiaris DN. Recent advances in oral pulsatile drug delivery. Recent Patents on Drug Delivery & Formulation, 2009; 3(1): 4963.
3. Amrutiya N, Bajaj A, and Madan M. Development of microsponges for topical delivery of mupirocin. Aaps Pharm.Sci.Tech., 2009; 10(2): 402409.
4. Sharma N, Agarwal D, Gupta M, and Khinchi M. A comprehensive review on floating drug delivery system. International Journal of Research in Pharmaceutical and Biomedical Sciences, 2011; 2(2): 428432.
5. Nokhodchi A, Raja S, Patel P, Asare-Addo K. The role of oral controlled release matrix tablets in drug delivery systems. Bioimpacts. 2012;2(4):175-87.https://doi.org/10.5681/bi.2012.027. Epub 2012 Nov 4. PMID: 23678458; PMCID: PMC3648939.
6. Grund, Julia & Körber, Martin & Bodmeier, Roland. (2013). Predictability of drug release from water-insoluble polymeric matrix tablets. European journal of pharmaceutics and biopharmaceutics : official journal of Arbeitsgemeinschaft fur Pharmazeutische Verfahrenstechnik e.V. 85. 10.1016/j.ejpb.2013.08.007.
7. Ayoub SS. Paracetamol (acetaminophen): A familiar drug with an unexplained mechanism of action. Temperature (Austin). 2021 Mar 16;8(4):351-371. doi: 10.1080/23328940.2021.1886392. PMID: 34901318; PMCID: PMC8654482.
8. Bacon TH, Hole JG, North M, Burnett I. Analgesic efficacy of sustained release paracetamol in patients with osteoarthritis of the knee. Br J Clin Pharmacol. 2002 Jun;53(6):629-36. doi: 10.1046/j.1365-2125.2002.01603.x. PMID: 12047487; PMCID: PMC1874331.
9. Nokhodchi A, Raja S, Patel P, Asare-Addo K. The role of oral controlled release matrix tablets in drug delivery systems. Bioimpacts. 2012;2(4):175-87. doi: 10.5681/bi.2012.027. Epub 2012 Nov 4. PMID: 23678458; PMCID: PMC3648939.
10. Shanmugam S. Granulation techniques and technologies: recent progresses. Bioimpacts. 2015;5(1):55-63. doi: 10.15171/bi.2015.04. Epub 2015 Feb 18. PMID: 25901297; PMCID: PMC4401168.
11. Özalp Y, Chunu JT, Jiwa N. Investigation of the Compressibility Characteristics of Paracetamol using "Compaction Simulator". Turk J Pharm Sci. 2020 Jun;17(3):249-253. doi: 10.4274/tjps.galenos.2019.38278. Epub 2020 Jun 22. PMID: 32636700; PMCID: PMC7336030.
12. Naik, Shreya & Somnache, Sandesh & Godbole, Ajeet M & Fernandes, Clecy. (2024). Enhancing paracetamol compressibility using the co-drying technique: Impact on tablet release profile from direct compression. German Journal of Pharmaceuticals and Biomaterials. 3. 1-8. 10.5530/gjpb.2024.3.7.
13. Gábor Vasvári, József Kalmár, Péter Veres, Miklós Vecsernyés, Ildikó Bácskay, Pálma Fehér, Zoltán Ujhelyi, Ádám Haimhoffer, Ágnes Rusznyák, Ferenc Fenyvesi, Judit Váradi,Matrix systems for oral drug delivery: Formulations and drug releaseDrug Discovery Today: Technologies,Volume 27,2018,Pages 71-80,ISSN 1740-6749, https://doi.org/10.1016/j.ddtec.2018.06.009.
14. Kundharaju, Ramakurthi & Kumar, Chirravuri. (2025). Formulation and In Vitro Evaluation of Paracetamol Sustained Release 1000 mg Tablets using Banana Starch As Dual-Action Control. Journal of Neonatal Surgery. 14. 210-219. 10.52783/jns.v14.2224.
15. Özalp Y, Chunu JT, Jiwa N. Investigation of the Compressibility Characteristics of Paracetamol using "Compaction Simulator". Turk J Pharm Sci. 2020 Jun;17(3):249-253. doi: 10.4274/tjps.galenos.2019.38278. Epub 2020 Jun 22. PMID: 32636700; PMCID: PMC7336030.
16. Ali, Heyam & Khan, Gazala & Elhaj, B.M. & Ajaji, Mai & Suliman, Rasha. (2016). Evaluation & formulation of paracetamol matrix sustained release tablets using natural polymers. Journal of Innovations in Pharmaceutical and Biological Sciences. 3. 85-91.
17. Ali, Heyam & Khan, Gazala & Elhaj, B.M. & Ajaji, Mai & Suliman, Rasha. (2016). Evaluation & formulation of paracetamol matrix sustained release tablets using natural polymers. Journal of Innovations in Pharmaceutical and Biological Sciences. 3. 85-91.
18. Vidyadhara S, Rao PR, Prasad JA. Development and in vitro kinetics of propanolol hydrochloride controlled release matrix tablets. Indian Pharm 2006;5:66-70.

19. Vidyadhara S, Choudhary YA, Murthy TE, Rao MV, Reddy KN. Influence of electrolyte on controlled release of Ambroxol hydrochloride from methocel matrix tablet. Pharma Review 2006:101-04.

20. Rahman Z, Ali M, Khar R. Design and evaluation of bilayer floating tablets of captopril. Acta Pharm 2006;56:49-57.

21. Afshan Mumtaz Hamdani, Idrees Ahmed Wani, Naseer Ahmad Bhat,Sources, structure, properties and health benefits of plant gums: A review,International Journal of Biological Macromolecules,Volume 135,2019,Pages 46-61,ISSN 0141-8130, https://doi.org/10.1016/j.ijbiomac.2019.05.103.

22. Vaishali N. Sonawane, Chaitali A. Yeola, Vijayraj N. Sonawane, Khemchand R. Surana1, Dhananjay M. Patil, Deepak D. Sonawane. Estimation of Paracetamol in various brands of Paracetamol Tablets and their Comparative Study. Asian Journal of Pharmaceutical Analysis. 2023; 13(3):155-1. doi: 10.52711/2231-5675.2023.00025

23. Chowdary, K.P.R and Ramya K: Recent research on co-processed excipients for direct compression a review, Pharmacie Globale, Int J. compr. Pharm. (2013) 4: 1.

24. Chaturvedi, Hitesh & Garg, Dr & Rathore, Udaibhan. (2022). POST-COMPRESSION EVALUATION PARAMETERS FOR TABLETS-AN OVERVIEW. EUROPEAN JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH. 4. 526-530.

25. Alam, Kamran. (2013). Formulation Development & Evaluation of caffeine tablets (200mg) by Direct Compression. Int. J. Drug Dev. & Res.. Vol. 5. 371-376.

26. Joachim Werther, Jens Reppenhagen,7 - Attrition in Fluidized Beds and Pneumatic Conveying Lines, Editor(s): Wen-Ching Yang, Fluidization, Solids Handling, and Processing, William Andrew Publishing, 1999, Pages 435-491, ISBN 9780815514275, https://doi.org/10.1016/B9780815514275.500090.(https://www.sciencedirect.com/science/article/pii/B9780815514275500090).

27. Abebe K, Beressa TB, Yimer BT. In-vitro Evaluations of Quality Control Parameters of Paracetamol Tablets Marketed in Gondar City, Northwest Ethiopia. Drug Healthc Patient Saf. 2020 Dec 21;12:273-279. doi: 10.2147/DHPS.S282420. PMID: 33376411; PMCID: PMC7762764.