REDVET - Revista electrónica de Veterinaria - ISSN 1695-7504
Vol 25, No.1 (2024)
http://www.veterinaria.org
Article Received- 22 Dec 2023 Revised: 20 March 2024 Accepted: 24 April 2024

Hydrotropic Solubilization: A Novel Approach For Enhancing Dissolution Of Antiemetic Drugs In Mouth Dissolving Tablets

Dr. Jitendra Gupta[1], Bhawna Sharma[2], Ittishree[3], Sangeet Kumar Sharma[3], Paras Gupta[4], Rajiv Yadav[5], Dr Surya Prakash Gupta[6], Dr. Neelam Pawar[7]*

[1]Institute of Pharmaceutical Research, GLA University, Mathura-281 406, U.P., India
[2]Department of Pharmaceutics, Madhyanchal Professional University (MPU)-Educational Institute, Bhopal-462 044, Madhya Pradesh, India
[3]Assistant professor, Hindu College of Pharmacy Sonipat- 131001 Haryana
[4]Associate Professor, United Institute of Pharmacy, Naini (Prayagraj) 211010
[5]Assistant Professor, Faculty of Pharmaceutical Sciences, Baba Mastnath University, Asthal Bohar, Rohtak, Haryana.
[6]Professor and Director, Rajiv Gandhi Institute of Pharmacy, Faculty of Pharmaceutical Science & Technology, AKS University, Sherganj Panna Road, Satna M.P.
[7]Department of pharmaceutical sciences, Chaudhary Bansilal University, Bhiwani Haryana

***Corresponding author:** Dr. Neelam Pawa
*****E mail : neelampawar5555@gmail.com

ABSTRACT
The purpose of this study is to investigate the hydrotropic solubilization approach as a means of improving the dissolution of the antiemetic medication aprepitant, which is known to be weakly water-soluble, in mouth-dissolving tablets (MDTs). In order to boost the drug's solubility, hydrotropic agents such as sodium benzoate and sodium acetate were utilized. Among these agents, sodium acetate at a ratio of 1:3 demonstrated the greatest solubility augmentation (12.053). The use of superdisintegrants such as sodium starch glycolate, crospovidone, and croscarmellose sodium allowed for the formulation of aprepitant solid dispersions into tablets that dissolve quickly. It was determined that the pre-compression characteristics, which included bulk density and flow properties, were within acceptable limits, which ensured that the tablet formation was satisfactory. Tablets were found to have suitable levels of hardness, friability, weight uniformity, and drug content after being subjected to compression testing. Formulation F7 had the highest level of performance among the tablets. In addition, F7 had the quickest disintegration time, which was only 38 seconds, and it reached practically total drug release within 15 minutes, according to first-order kinetics. Hydrotropic solubilization has shown to be a successful approach for enhancing the solubility and bioavailability of medications that are weakly water-soluble in MDTs, as demonstrated by this study.

Keywords: Hydrotropic Solubilization, Antiemetic Drugs, Mouth Dissolving Tablets, Enhanced Dissolution, Drug Solubility, Pharmaceutical Formulation.

1. INTRODUCTION

A larger percentage of weakly water soluble or water insoluble medications are included in both the US and Indian pharmacopoeias [1]. Water solubility and other poor biopharmaceutic characteristics are the primary cause of the failure of new medication development. For drug development, solubility is one of the most crucial physical-chemical characteristics. Poor solubility and lipophilicity are two characteristics of several recently produced pharmacological compounds. Different organic solvents, including methanol, chloroform, dimethyl formamide, and acetonitrile, are utilized to solubilize these weakly water-soluble medications [2]. The use of these organic solvents is not without its drawbacks, though, such as their hefty price tags, instability, environmental impact, and potential toxicity. So, the hydrotropic agent may be used, which is a solvent that is safe, cheap, and good for the environment [3]. Hydrotropy is a solubility phenomenon that happens when a second solute is introduced in large amounts and its aqueous solubility increases. Sodium benzoate, sodium salicylate, urea, sodium citrate, nicotinamide, and sodium acetate in a concentrated water-based hydrotropic solution are some examples.
An anionic organic salt was categorized by use of a hydrotropic agent. A hydrotropic aromatic ring or ring system and an anionic group are the two main components of hydrotropic salts, as shown by chemical studies of classic Neuberg's salts [4]. There is a lot of water solubility due to the anionic group, which could not even affect the phenomena much [5].

1.1. Solubility

A substance's solubility properties can be investigated using both quantitative and qualitative methods. A solute's concentration in a saturated solution at a particular temperature is its quantitative definition, which gives an exact indication of how much solute may dissolve in a particular solvent [6]. Because one milliliter of solvent is required to dissolve one gram of solute, pharmacopoeial standards often express this in terms of grams of solute per milliliter of solvent. For many purposes, this accurate assessment is essential, particularly in the pharmaceutical industry where a drug's solubility can

REDVET - Revista electrónica de Veterinaria - ISSN 1695-7504
Vol 25, No.1 (2024)
http://www.veterinaria.org
Article Received- 22 Dec 2023 Revised: 20 March 2024 Accepted: 24 April 2024

have a substantial impact on its bioavailability and therapeutic effectiveness. Conversely, the qualitative dimension of solubility concerns the character of the solute-solvent interaction that results in the creation of a uniform molecular dispersion. At the molecular level, this dispersion is the product of the solvent and solute's spontaneous interactions, which lead to a homogenous mixture [7]. Additionally, in situations when precise solubility values are not easily accessible, pharmacopoeias use broad terminology that denote a specified range of solubility. By easing their usage in formulation and therapeutic contexts, these categories aid practitioners in understanding the solubility qualities of different substances. All things considered, effective use in a variety of scientific and commercial domains requires a thorough grasp of solubility, including both its quantitative measures and qualitative interactions [8].
A few wide factors that might influence solubility incorporate molecule size, shape, and surface region; physical and compound qualities of the medication; solvents; temperature; pH of the medium; and the utilization of surfactants [9].

Table 1: System of categorization for biopharmaceutics

Classification	Characteristics
BCS 1	Highly soluble, highly permeable
BCS 2	Low soluble, highly permeable
BCS 3	Highly soluble, Low permeable
BCS 4	Low soluble, Low permeable

Drugs might be characterized into four biopharmaceutical classes in view of their solubility, as displayed in Table 1. Like that, we can arrange the drug's solubility as per its porousness across layers and its solubility in water [10].

1.2. Need For Solubility

The absorption of medications in the gastrointestinal system is affected by a multitude of factors, such as the drug's low water solubility and membrane permeability. Oral medicine cannot cross the gastrointestinal tract (GIT) membrane unless it dissolves in the digestive fluids. Solubility and rate of dissolution should be enhanced for drugs that have low water solubility [11]. Consequently, the correct doses of the medicine must be available at the correct sites of action. A medicine's bioavailability and solubility may affect how well it works therapeutically [12]. To get the right concentration in the systemic circulation for the pharmacological reaction, the solubility of the medicine is the most important component. Poor bioavailability prevents the commercialization of 40% of lipophilic medicine candidates. A high dose was required to achieve the desired pharmacological effect. Medications that have a low solubility in water can have their solubility improved using various solubilization techniques [13].

2. PROCESS OF SOLUBILIZATION

Interaction between a solute and a solvent causes a homogenous solution to develop during the solubilization process [14]. It starts with the introduction of the solute, which is generally a solid, to the solvent, which is usually a liquid. Forces of attraction, including hydrogen bonds, dipole-dipole interactions, or Van der Waals forces, start to become important as soon as the solute and solvent molecules come into contact. These forces aid in the dispersion of solute molecules throughout the solvent by facilitating the breakdown of intermolecular connections within the solute [15]. The solubilization process is greatly influenced by variables including temperature, agitation, and the makeup of the solvent and solute. For example, raising the temperature often improves solubility by giving the necessary energy to overcome interactions between the solution and the solute. Stirring the mixture can also aid in more uniformly dispersing the solute throughout the solvent, hastening the dissolving process [16]. The amount of solubilization is also determined by the molecular size and polarity of the solvent and solute, among other chemical characteristics. When solubilization is successful, the solute eventually finds itself in a stable solution with uniform distribution, which enables it to efficiently engage in a variety of chemical reactions and biological activities.
This involves the following steps [17]:
1. In the solvent, holes might open.
2. The solute's intermolecular or interionic bonds breaking.
3. The solid's molecules separate from the bulk.
4. The solid molecules that have been released are incorporated into the solvent's hole.
5. The solubilization process, which is the result of this interaction between the solvent and the solute molecule or ions, may be the source of the idea of holes or cavities in liquids.

REDVET - Revista electrónica de Veterinaria - ISSN 1695-7504
Vol 25, No.1 (2024)
http://www.veterinaria.org
Article Received- 22 Dec 2023 Revised: 20 March 2024 Accepted: 24 April 2024

Figure 1: Steps in the solubilization process

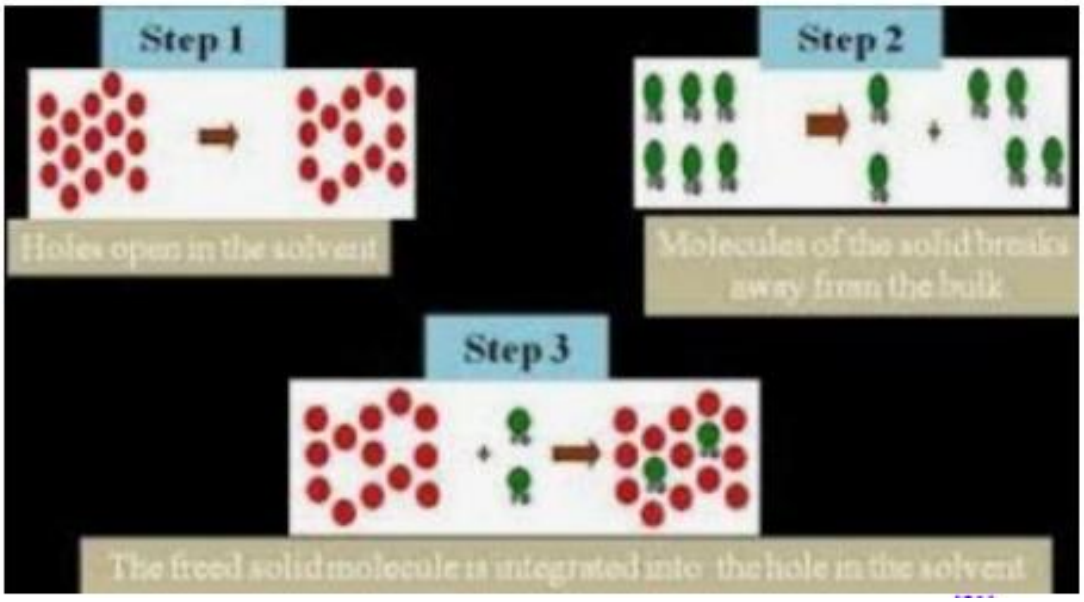


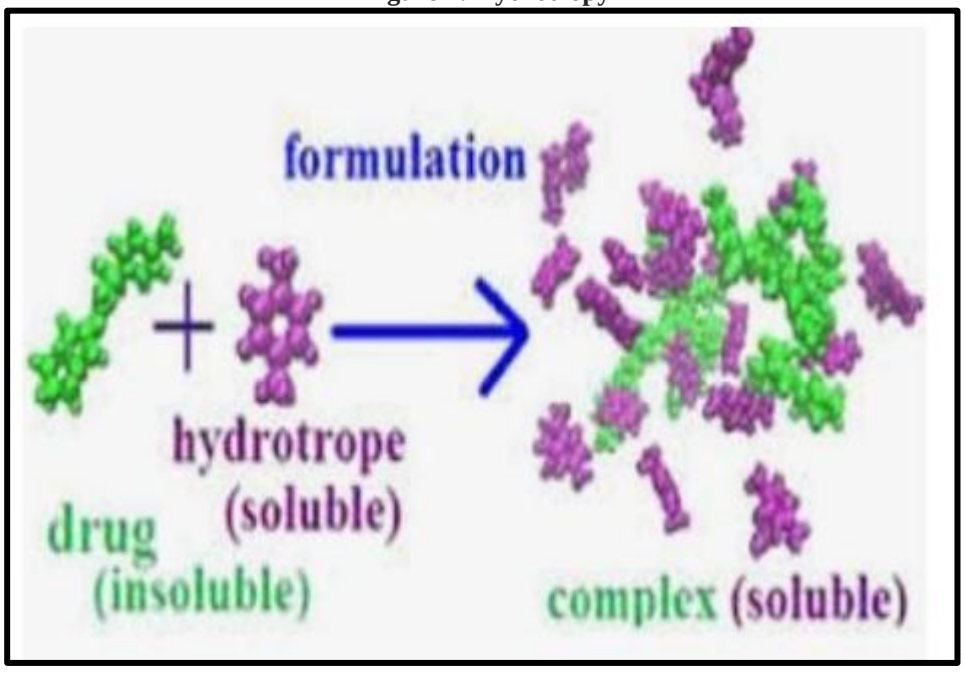
Figure 1 shows three potential steps that might be utilized to construct the whole procedure:

1. In order to transfer a molecule from the solute phase to the vapour phase, it is necessary to first break the bonds between nearby molecules [18].
2. Consequently, the solvent forms pores that can accommodate the molecules of the solute.
3. Finally, solute molecules are introduced into the solvent through the hole in the third and final phase.

2.1. Hydrotropy

Hydrotropy is a novel and unparalleled method of solubilization. Here, the use of certain chemical substances known as hydrotropes is utilized to modify sparingly soluble solutes' water solubility by a factor of many under typical circumstances [19].

Figure 2: Hydrotropy



,

At certain concentrations, the molecules become more soluble in water because they form organized assemblies of hydrotropic molecules [20]. Figure 2 shows that these substances may have surface-active compounds that are soluble in water and can enhance the solubility of organic solutes such acids, lipids, esters, ketones, hydrocarbons, and aldehydes.

REDVET - Revista electrónica de Veterinaria - ISSN 1695-7504
Vol 25, No.1 (2024)
http://www.veterinaria.org
Article Received- 22 Dec 2023 Revised: 20 March 2024 Accepted: 24 April 2024

3. MATERIAL AND METHOD

3.1. Selection and Reparation of Hydrotrope for Insufficiently Water-Soluble Drug hospitable

The dissolving media, which consisted of distilled water, solutions of sodium acetate, sodium benzoate, and ascorbic acid at increasing concentrations, and excess drug were added one at a time to determine the equilibrium solubility at room temperature. Next, the mixtures were subjected to mechanical shaking for 12 hours at a temperature of 28°±1°C. After that, they were given 24 hours to equilibrate before being centrifuged for 5 minutes at 2000 rpm. Whatman filter paper (No. 41) was used to filter out the obtained supernatant in each case. Spectrophotometric examination was performed at 264 nm after each filtrate was properly diluted.

Table 2: varying drug-to-hydrotrope ratios

S No.	Drug/Hydrotrope ratio	Hydrotrope
1	1:1:1.5	Sodium benzoate/Sodium acetate
2	1:2:2.5	Sodium benzoate/Sodium acetate
3	1:3:3.5	Sodium benzoate/Sodium acetate

3.2. creation of the Aprepitant fast-dissolving tablet formulation

The following ingredients were used to make fast-dissolving tablets of Aprepitant solid dispersion (equivalent to 10 mg): mannitol, aspartame, crospovidone, croscarmellose sodium, an alcoholic solution of polyvinyl pyrrolidone (PVP K-30), aerosil, magnesium stearate, and sodium starch glycolate. Each individual ingredient was first passed through a 100-mesh filter before being combined. It was necessary to add a sufficient quantity of PVP K-30 (10% w/v) alcoholic solution to the mixture of medicine and other ingredients before stirring to form a cohesive mass. The first step was to granulate the wet bulk using sieve number 12, and then to regranulate it when it dried using sieve number 16. Next, the granules from each formulation were vacuum-dried for 12 hours at 60°C in a Vertex VT4810 oven.

The infrared moisture balance revealed that the granules' final moisture content ranged from 1% to 2%. The menthol waned as the drying process caused the tablet's surface to become more porous. Grind the dry granules with some talc and magnesium stearate on a Rimek-I rotary tablet machine with flat face round tooling until you get tablets.

Table 3: creation of many batches of tablets that dissolve quickly

F Ingredients (mg)	F1	F2	F3	F4	F5	F6	F7	F8	F9
Aparepitant solid dispersion 80 milligrams (320 milligrams)	300	300	300	300	300	300	300	300	300
SSG	10	20	30	-	-	-	-	-	-
CP	-			10	20	30	-	-	-
CCS	-	-	-	-	-	-	10	20	30
Tale	10	10	10	10	10	10	10	10	10
Mg. Scearate	10	10	10	10	10	10	10	10	10
Lactose	20	10	-	20	10	-	20	10	-
Mannitol	70	70	70	70	70	70	70	70	70
Total	**420**	**420**	**420**	**420**	**420**	**420**	**420**	**420**	**420**

3.3. Evaluation of precompression parameter

- **Point of rest (θ):** Frictional powers in grains or powder that are not firmly pressed not set in stone by ascertaining their point of rest. The outer layer of a granule or powder heap can be at a point more noteworthy than this concerning the flat plane.

$$\text{Tan } \boldsymbol{\theta} = h/r$$
$$\boldsymbol{\theta} = \tan^{-1}(h/r)$$

where Θ represents the point of rest, r for the span, and h for the level.
A channel was joined to a stage at a proper level, and granules were permitted to go through it. To find the point of rest, the resulting estimations of the granule store's level and range were taken.

- **Mass thickness:** The implications of tapped mass thickness (to be determined) and free mass thickness (LBD) were uncovered. A 50 ml estimating compartment was loaded up with a careful load of granules. The accompanying computations were utilized to gauge the LBD and yet to be decided, which were gotten by tapping the chamber multiple times on a smooth, firm hardwood surface.

$$\text{LBD (Loose Bulk Density)} \frac{\text{Mass of Powder}}{\text{Volume of Packing}}$$

REDVET - Revista electrónica de Veterinaria - ISSN 1695-7504
Vol 25, No.1 (2024)
http://www.veterinaria.org
Article Received- 22 Dec 2023 Revised: 20 March 2024 Accepted: 24 April 2024

$$\text{TBD (Tapped Bulk Density)} = \frac{\text{Mass of Powder}}{\text{Tapped Volume of Packing}}$$

- **Carr's Compressibility record:** To decide the % compressibility of the powder blend, Carr's compressibility file was determined utilizing the accompanying recipe:

$$\text{Carr;s Index \%} = \frac{\text{TBD} - \text{LBD}}{\text{TBD}} \times 100$$

- **Hausners proportion:** The accompanying condition is utilized to contrast the tapped thickness with the mass thickness: -

The Housner's proportion is the result of the tapped mass thickness and the free Mass thickness For further developed stream attributes, the Hausner proportion ought to be under 1.25.

3.4. Assessment of post pressure Boundary

The structure and shade of the pills

Uncoated tablets were seen utilizing a focal point to decide their structure, and by presenting them to light, their variety was noted.

- **Thickness test :** Three tablets were arbitrarily chosen from every formulation, and their thickness was evaluated autonomously. The worth is given in millimeters and its standard still up in the air. To decide the tablet's thickness, a dial-caliper (Mitutoyo, Japan) was used. Check for changes in body weight Twenty tablets were arbitrarily chosen from every formulation, and their typical not entirely settled. We contrasted the normal load with the information got from gauging every tablet independently. The US Pharmacopeia considers a modest quantity of variety in tablet weight. This is the scope of suitable weight variance rates:

- **Hardness test :**The tablet's hardness was estimated utilizing the Pfizer hardness analyzer, and the outcomes were accounted for in kg/cm2.

- **Friability test:** The hardware was run for four minutes at a speed of 25 cycles each moment. We determined the level of friability subsequent to taking the pills out, tidying them, and afterward gauging them once more. The mass misfortune in percent was assessed for friability utilizing the condition.
  % Friability = (Loss in Weight / Initial Weight) × 100

In the event that the weight reduction of the tablets is under 1%, the test is thought of as effective.
Medicine content consistency: This test is vital for tablets with a functioning fixing content of 10 mg or less. We sonicated the blend for 20 minutes until all of the medicine filtered out of the mind boggling, which included finely powdering what might be compared to 5 mg of ten arbitrarily chosen tablets (F1 to F9) utilized in the formulations. Whatman channel paper No. 41 was in this manner used to channel the blend. A 100 mL weakening of this arrangement was produced using 2 mL of the first arrangement utilizing phosphate cushion (pH 6.8). Spectrophotometry was then used to decide the drug fixation at 264 nm.

3.5. Dissolution rate studies

A drug discharge test was directed in vitro on the fabricated tablets. Prescriptions were tried for discharge utilizing a USP XXII oar type dissolution gear. The dissolution analyze utilized 900 ml of break up media that was kept up with at 37±0.2, C and mixed at 75 rpm. In various settings, the expected utilization of the reenacted liquids was as per the following:
To compensate for the volume misfortune, 10 mL of phosphate cradle (pH 6.8) was added to the example. A 264 nm spectrophotometer was utilized for the spectrophotometric assessment of the extricated materials. To decide when the medication will be delivered, the Apepitant Standard Bend was utilized.

4. RESULTS AND DISCUSSION

The investigation into the formulation and characterisation of mouth dissolving tablets (MDTs) for an antiemetic medicine utilizing the hydrotropic solubilization approach shows a number of significant discoveries about the augmentation of solubility, the drug content, and the quality of the tablets.

Solubility Enhancement: Based on the information shown in Table 4, it is clear that hydrotropic agents have an effect on the solubility of the antiemetic medication. After conducting tests with sodium benzoate and sodium acetate in varying proportions, it was discovered that sodium acetate exhibited a greater degree of solubility enhancement in comparison to sodium benzoate. To be more specific, a ratio of sodium acetate to water resulted in the maximum solubility improvement of 12.035 showing that it performed exceptionally well in terms of improving drug solubility. The findings of this study are consistent with those of earlier research that suggests hydrotropic compounds have the potential to greatly improve the solubility of medications that are not very water-soluble.

REDVET - Revista electrónica de Veterinaria - ISSN 1695-7504
Vol 25, No.1 (2024)
http://www.veterinaria.org
Article Received- 22 Dec 2023 Revised: 20 March 2024 Accepted: 24 April 2024

Drug Content: The findings of the drug content analysis are presented in Table 5, which is a key component in verifying that the MDTs are effective in their therapeutic applications. At a percentage of 97.80 percent, the quantity that was discovered in the pills was quite near to the amount that was anticipated. This implies that the medication content is homogeneous and consistent throughout all of the formulations, which is essential for ensuring that the dose is accurate.

Post-Compression Parameters: All of the formulations were found to have acceptable levels of drug content, as well as appropriate levels of hardness, friability, and weight variation, according to the results of the post-compression tests reported in Table 6. Formulation F7, in particular, demonstrated the greatest drug concentration, as well as good hardness and friability, which suggests that it possesses robust mechanical qualities and stability.

Pre-Compression Parameters: The results shown in Table 7 concerning the pre-compression properties show that all of the formulations have excellent bulk density, Carr's index, Hausner's ratio, and angle of repose values. These variables greatly affect the flow characteristics and compressibility of the powder mix, which is crucial in determining the quality of the tablets made from the powder blend. Lower values of the Carr's Index and Hausner's Ratio are often indicative of formulations with improved flowability and compressibility, both of which are essential for the effective processing of the materials into high-quality tablets. The findings emphasize how crucial it is to maximize these pre-compression properties in order to produce tablet formulations that are acceptable and satisfy the requirements for use in pharmaceutical applications.

Disintegration Time: According to Table 8, formulation F7 had the quickest disintegration time, which was 38 seconds. This is advantageous for MDTs because it enables fast dissolution in the oral cavity, which is the primary goal of medication delivery systems. There is a correlation between shorter disintegration durations and a speedier commencement of action, which is especially advantageous for agents that treat nausea and vomiting.

Drug Release: The profile of the drug release that occurs with the improved formulation F7 is presented in Table 9. According to the release statistics, F7 was able to accomplish virtually entire drug release within fifteen minutes, which is evidence of its effective dissolving performance. The results of the regression analysis presented in Table 10 indicate that the drug release from formulation F7 follows first-order kinetics, which is often suggestive of a regulated release profile. The R2 value for the first-order kinetics is 0.980.

Table 4: Determination of enhancement of solubility in prepared solid dispersion

S No.	Drug/ Hydrotrope ratio	Hydrotrope	Solubility Enhancement	
			Absorbance	Solubility Enhancement
1	1:1	Sodium benzoate	0.120	3.025
2	1:2	Sodium benzoate	0.220	5.125
3	1:3	Sodium benzoate	0.350	9.265
4	1:1	Sodium benzoate	0.200	5.550
5	1:2	Sodium benzoate	0.361	9.123
6	1:3	Sodium benzoate	0.469	12.035
Abs. of standard			0.040	

Table 5: Results of determination of drug content

S No.	Amount Percentage	Amount Found	%
1	11	8.26	90.23

Table 6: Aftereffects of post-pressure boundaries, all things considered,

F code	Hardness test (kg/cm^2)	Friability (%)	Weight variation (%)	Thickness (mm)	Drug Content (%)
F1	3.3 ± 0.2	0.658 ± 0.074	405 ± 4	1.45 ± 0.05	97.85 ± 0.15
F2	3.2 ± 0.2	0.732 ± 0.023	403 ± 2	1.52 ± 0.03	98.85 ± 0.22
F3	3.2 ± 0.3	0.685 ± 0.015	400 ± 5	1.49 ± 0.02	98.65 ± 0.16
F4	3.3 ± 0.4	0.712 ± 0.012	398 ± 3	1.53 ± 0.01	97.12 ± 0.17
F5	3.3 ± 0.2	0.785 ± 0.022	396 ± 4	1.52 ± 0.03	98.78 ± 0.36
F6	3.4 ± 0.3	0.658 ± 0.014	398 ± 6	1.53 ± 0.02	98.65 ± 0.25
F7	3.3 ± 0.2	0.612 ± 0.036	402 ± 3	1.48 ± 0.04	99.87 ± 0.27
F8	3.4 ± 0.3	0.668 ± 0.047	398 ± 2	1.52 ± 0.04	97.65 ± 0.15
F9	3.2 ± 0.2	0.652 ± 0.032	403 ± 4	1.47 ± 0.03	97.12 ± 0.36

REDVET - Revista electrónica de Veterinaria - ISSN 1695-7504
Vol 25, No.1 (2024)
http://www.veterinaria.org
Article Received- 22 Dec 2023 Revised: 20 March 2024 Accepted: 24 April 2024

Table 7: Aftereffects of pre-pressure boundaries of Aprepitant

Formulation code	Parameters				
	Loose Bulk density(gm/ml)	Tapped bulk density(gm/ml)	Carr's Index (%)	Hausner's Ratio	Angle of Repose
F1	0.350	0.414	22.03	1.300	44º
F2	0.360	0.446	22.50	1.250	43º
F3	0.345	0.436	21.36	1.360	43º
F4	0.322	0.419	22.14	1.300	44º
F5	0.365	0.498	23.00	1.260	45º
F6	0.347	0.400	21.56	1.245	44º
F7	0.336	0.498	24.16	1.300	43º
F8	0.351	0.468	22.36	1.256	45º
F9	0.392	0.450	23.45	1.362	45 º

Table 8: Aftereffects of in vitro breaking down season, all things considered,

Formulation code	Disintegration Time (sec.)
	84±2
F1	77±5
F2	71±2
F3	60±6
F4	54±3
F5	53±9
F6	40±3
F7	44±3
F8	66±5
F9	56±4

Table 9: Data on drug release for formulation F7 that is optimized

Time (min)	Square Root of Time(h)1/2	Log Time	Cumulative* % Drug Release	Log Cumulative % Drug Release	Cumulative % Drug Remaining	Log Cumulative % Drug Remaining
1	1	0	62.31	1.800	35.12	1.550
5	2.230	0.700	84.12	1.954	12.16	1.103
10	3.150	1	95.13	1.983	3.16	0.500
15	3.840	1.160	99.30	1.923	0.90	-0.060

Table 10: Regression analysis data

Batch	Zero Order	First order
	R^2	R^2
F7	0.765	0.980

5. CONCLSUION

The investigation on the use of hydrotropic solubilization to improve the absorption of Aprepitant in oral dissolving tablets has shown encouraging findings. The solubility profile of the medication was considerably enhanced by sodium acetate, which performed better than sodium benzoate and achieved the greatest solubility at a 1:3 ratio. The development of the formulation produced tablets that exhibited high uniformity and consistency, with an average drug content of 97.80%, meeting quality criteria. Evaluations conducted prior to compression revealed positive flow characteristics, while tests conducted after compression validated the tablets' resilience with respectable hardness and friability. With a 38-second disintegration time and almost full drug release in 15 minutes, formulation F7 stood out for its potential for a quick commencement of action, which is important for antiemetic therapy. Overall, the findings demonstrate that the hydrotropic solubilization method is useful in improving the dissolving properties of weakly water-soluble medications like Aprepitant, opening the door to more favorable therapeutic effects in oral formulations.

REFERENCES

1. AbouSamra, M. M., Salama, A. H., Awad, G. E., & Mansy, S. S. (2020). Formulation and evaluation of novel hybridized nanovesicles for enhancing buccal delivery of ciclopirox olamine. AAPS PharmSciTech, 21, 1-12.

2. Banerjee, T., Banerjee, B., & Jain, P. (2012). Spectrophotometric estimation of lornoxicam and paracetamol tablet dosage form using hydrotropic solubilizing agent. International Journal of ChemTech Research, 4(1), 232-239.
3. Bhalani, D. V., Nutan, B., Kumar, A., & Singh Chandel, A. K. (2022). Bioavailability enhancement techniques for poorly aqueous soluble drugs and therapeutics. Biomedicines, 10(9), 2055.
4. Chaudhary, A., Rathore, S. S., & Patel, A. R. (2012). Hydrotropic Solubilization: An Effective Tool for Enhancing Solubility of Poorly Soluble Drugs. International Journal of Pharmaceutical Sciences and Research, 3(9), 3132-3140.
5. Chinwala, M. (2020). Recent formulation advances and therapeutic usefulness of orally disintegrating tablets (ODTs). Pharmacy, 8(4), 186.
6. Deshmukh, P., Nimkar, S., Phuse, A., Ruikar, D., & Bonde, D. (2024). A Systemic Review on Techniques of Solubility Enhancement for Poor Water-Soluble Drugs. Asian Journal of Pharmaceutical Research and Development, 12(3), 247-256.
7. Gupta, A., Paudwal, G., Dolkar, R., Lewis, S., & Gupta, P. N. (2022). Recent advances in the surfactant and controlled release polymer-based solid dispersion. Current Pharmaceutical Design, 28(20), 1643-1659.
8. Gupta, V., Singh, S. P., & Sharma, S. K. (2015). Application of Hydrotropic Solubilization Technique in Formulation of Oral Tablets: An Overview. Journal of Applied Pharmaceutical Science, 5(4), 34-41.
9. Jadhav, S. P., Singh, S. K., & Chawra, H. S. (2023). Review on Nanosuspension as a Novel Method for Solubility and Bioavailability Enhancement of Poorly Soluble Drugs. Advances in Pharmacology and Pharmacy, 11(2), 117-30.
10. Liu, Z., Shi, C., Fang, Y., Zhao, H., Mu, Y., Zhao, L., & Shen, L. (2023). A comprehensive understanding of disintegrants and disintegration quantification techniques: From the perspective of tablet microstructure. Journal of Drug Delivery Science and Technology, 104891.
11. Maheshwari, R. K., Deswal, S., Tiwari, D., Ali, N., Pothen, B., & Jain, S. (2007). Novel spectrophotometric estimation of frusemide using hydrotropic solubilization phenomenon. Indian Journal of Pharmaceutical Science, 69(6), 822-824.
12. Maheshwari, R. K., Lakkadwala, S., Vyas, R., & Ghode, P. (2010). Spectrophotometric determination of naproxen tablets using niacinamide as hydrotropic solubilizing additive. Journal of Current Pharmaceutical Research, 4, 11-14.
13. Padiyar, A., Agrawal, O. P., Rajpoot, K., & Tekade, R. K. (2020). Hydrotropy, mixed hydrotropy, and mixed solvency as trending concept for solubilization of lipophilic drugs. In The Future of Pharmaceutical Product Development and Research (pp. 145-178). Academic Press.
14. Patel, M. A., & Patel, A. G. (2016). Development and Characterization of Mouth Dissolving Tablets of Antiemetic Drug Using Hydrotropic Solubilization. Pharmaceutica Analytica Acta, 7(6), 257-264.
15. Rao, P. R., & Lamba, S. A. (2015). Formulation and Evaluation of Mouth Dissolving Tablets of Antiemetic Drug Using Hydrotropic Solubilization Technique. Asian Journal of Pharmaceutical and Clinical Research, 8(3), 114-118.
16. Rashid, M., Malik, M. Y., Singh, S. K., Chaturvedi, S., Gayen, J. R., & Wahajuddin, M. (2019). Bioavailability enhancement of poorly soluble drugs: the holy grail in pharma industry. Current Pharmaceutical Design, 25(9), 987-1020.
17. Revathi, R., Ethiraj, T., Saravanan, V. S., Ganeshan, V., Saranya, V., & Sengottuvel, T. (2010). New spectroscopic determination of nifedipine using hydrotropic solubilization. International Journal of Pharmaceutical Sciences, 2(4), 74-76.
18. Shukla, R., Patel, A., Soni, M. L., Modi, V., & Jaliwala, Y. A. (2008). Quantitative spectrophotometric estimation of cefadroxil using hydrotropic solubilization technique. Asian Journal of Pharmaceutics, 2(3), 146-147.
19. Sopyan, I., Adiningsih, N., Megantara, S., & Marvita, S. S. (2023). Solubility Enhancement of Carvedilol by Solid Dispersion Technique Using Sodium Alginate, Guar Gum, Xanthan Gum, and Locust Bean Gum as Polymers. Indonesian Journal of Chemistry, 23(2), 349-357.
20. Subhi, S. S., Thamrook, S., Manohar, R. D., & Mathan, S. (2020). Self Micro Emulsifying Mouth Dissolving Film (SMMDF): A Novel Formulation for Poorly Water-Soluble Drugs. Journal of Pharmaceutical Sciences and Research, 12(7), 964-969.