Journal of Population Therapeutics & Clinical Pharmacology

RESEARCH ARTICLE
DOI: 10.53555/5n1j7b63

DEVELOPMENT AND EVALUATION OF PATIENT-FRIENDLY DISPERSIBLE TABLETS FOR PEDIATRIC AND GERIATRIC DRUG DELIVERY

Mr. Kiran M. Adchitre*[1], Mr. Nadim S. Khan[2], Mr. Hemant B. Bansode[3], Sachin S. Pingale[4]

[1*]Lecturer, Adarsh Shikshan Prasarak Mandal's, D. Pharmacy institute, Osmanabad.
[2,] Assistant Professor, ASPMs K. T. Patil College of Pharmacy, Osmanabad.
[3]Assistant Professor, SVERI's College of Pharmacy, Pandharpur.
[4]Assistant Professor, Late Laxmibai Phadtare College of Pharmacy, Kalamb Walchandnagar.

***Corresponding Author:** Mr. Kiran M. Adchitre[1]
[1]Lecturer, Adarsh Shikshan Prasarak Mandal's, D. Pharmacy institute, Osmanabad

ABSTRACT
The production of a pharmaceutical that is suitable for use by humans should be the main focus of any endeavour that is geared toward the development of a drug delivery system (DDS). A tablet that can be easily dispersed in the mouth reduces the need for several formulations of the same medicine. The rapid dispersible drug delivery system was developed so that people who needed help taking their medicine may do it in a way that was reliable and consistent. Over the last several years, there has been a discernible increase in research efforts directed toward the development of drug delivery systems that have a pleasant flavour, are easy for patients to use, and are risk-free for both young people and older people. Due to the fact that their bioavailability is higher than that of standard oral dose forms, rapid dispersible and dissolving formulations are considered to be the best way of administration when it comes to dosing. The primary objective of the research being conducted in this field is to identify an original technique for the production of quick- dissolving tablets. Increasing the active ingredient's solubility, improving the drug's organoleptic qualities, and encouraging patients to take their medication are some of the suggestions that have been made here. These are just some of the ways that the bioavailability of the active ingredient can be increased in vivo. Due to the fact that this formulation was developed for people of all ages, including children and the elderly, it may be beneficial to use.

Keywords: Dispersible tablets, Pediatric, Geriatric drug delivery.

Introduction:
Challenges in Development of Pediatric Medicines Formulations
It is normal practise to provide a wide range of drugs to children, including liquids and suspensions in addition to pills, chewable tablets, and oral disintegrating tablets. This is because it is easier for children to consume these forms of medication (ODTs). It is not recommended by paediatricians to give pills to children under the age of two. Instead, liquids or suspensions should be used to provide the medication to young children. Patients who are older than 2 years old should be given medications that are taken by mouth, including chewable tablets and ODT. Children older than six

years old should take their medicine in the form of chewing gum, pills, or capsules. Children aged 0–3 years and children aged 4–12 years should not get more than 10 millilitres. A significant amount of research and development effort is now being put into the creation of solid oral drugs for children that are appropriate for their age range. This study looks at the pharmacological properties, dose, pharmacokinetics, and pharmacodynamics of bitter taste blockers. It also investigates the safety of various excipients. The medicine has to have a pleasant flavour, not be too rough, be of a small size, dissolve quickly, and be able to provide the appropriate quantity.

Age Related Factors

People have a more good impression of those who are skilled in the administration of drugs because of their increased experience as they become older. It is possible to give the patient different amounts of medicine in patient-specific dosage forms, and the amount given depends on the patient's age. The usage of this drug in children is not only beneficial but also completely safe. Taking into consideration its age and level of development, it also contributes to the prevention of prescription mistakes.

Medical Adherence

There are a few strategies that have shown to be effective in getting children to take their medication, including giving just a single dose per day, creating pharmaceuticals that have a sweet flavour, and using liquid dosage forms in addition to or in place of solid dosage forms. It is a good idea to include a child of any age in the process of picking and taking their prescription, even if they are very young. Medicines that are formulated as ODT or dispersible tablets, granules and micro, skin creams, or modified release formulations are all forms that are simple to consume.

Other than Label and Unauthorized use of Medicines

Medication that has been incorrectly labelled or that was acquired illegally must be returned. Medical research into the development of medications for children is hampered by factors that are both practical and ethical. As a consequence of this, less than one-third of all drugs have been granted approval for use in children. It is conceivable that a drug that has been approved by the FDA may not be suitable for a patient's age group due to the manner in which it was manufactured, the dose that it was prescribed, or the chemicals that it included. As long as the children are under the care of medical experts, it is permissible for such doctors to give the children adult medications.

Usage of Delivery Hurdles

The fact that tablets and capsules do not exist in a variety of doses is one of the most significant problems. It is inappropriate for anybody above the age of 18 to provide them to anyone under the age of 18, and children under the age of four should never be given them. It is possible that the dose will need to be adjusted for a bottle of drink that has been opened or for a meal that has already been cooked. Pediatricians may be willing to use oral solutions and syrups, but because of the risk of administering the wrong dose, these preparations cannot be stored for extended periods of time. Tablets such as dispersible and bubbly tablets, which may exist in both solid and liquid states, are examples of products that fit into this category.

Pediatric Dosage Form

It is challenging to develop a drug for children that is successful across the board for children of all ages. The ultimate goal should be the development of single-dose formulations that treat several illnesses.

Convenient and Reliable Administration
Depending on the child's age and needs, the dosage may need to be adjusted. Parent-friendly dosage forms for paediatric medications should be available in easily-administered dosage forms. It should only need a little modification in dose. Provide medicine in little and frequent dosages is crucial.

Acceptability and Palatability
Several factors are taken into consideration when determining how well a medication is received, including how well it is packaged, how well it is labelled, and how good the drug tastes. The term "palatability" refers to the degree to which a medicine's flavour, fragrance, dosage, volume, and texture are all accepted by the patient.

Minimum Dose Frequency
After twice daily administration, it has an impact on the dosage arrangements for the caregiver and the child (for example, at school)

Excipients
When selecting excipients, it is important to make a difficult decision since the FDA's inactive ingredients guide (IIG) and the list of "generally regarded as safe" excipients provide no information on their safety when used in paediatric medications. Patients in the paediatric population may have adverse reactions to the excipients used in adult drugs. Because of the importance of performance, stability, palatability, microbiological control, and dose consistency in pharmaceutical formulations, it is necessary to employ a bare minimum of components and a bare minimum of each ingredient. The excipients used in liquid dosage forms are the most common cause of unfavourable side effects in this population.

Evaluating Palatability
It is necessary to use palatability testing in the development of innovative paediatric dose forms. Palatability may be determined using a variety of approaches, including electronic tongues, adult taste panels, and even the rat lickometer model, which is based on the licking of rats. An adult sensory panel as well as clinical study involving children are required for flavour analysis**.**

Identification of Amoxicillin:
Melting Point:
The open capillary technique was used in order to determine the melting point of pure amoxicillin. The capillary was sealed with fusion on one side, and a succession of tapes were used to fill it with liquid amoxicillin on the other side. The melting point apparatus included a computer, and the capillary was placed inside of it to determine the temperature at which it melted. The apparatus was programmed to increase the temperature of the water that was being heated at a pace of one thousand degrees Celsius per minute automatically. To better see the increase in temperature, a magnifying lens was used. When did the drug begin to melt, and at what temperature did this happen? It was committed to paper.

Infrared absorption spectrophotometer:
In order to determine whether or not the sample contains amoxicillin, an infrared absorption spectrometer was used. The sample was dried out in an oven using hot air in an effort to remove any remaining moisture that may have been present. The sample was made by

combining potassium bromide with a mortar and pestle to create the sample. In order to get information on the sample's spectrum, it was introduced into the FT-IR instrument and scanned from a range of 400 to 4000 cm-1. It was determined how accurate the collected IR spectra were by comparing them to the standard IR spectrum of amoxicillin.

Ultra visible spectrophotometer:
A solution with a concentration of 50g/ml was created in water, and a scanning microscope was used to examine the solution in the range of 200–400 nm. The UV spectrum of amoxicillin was utilised as a reference, and it was compared to the spectrum that was generated after it had been created.

Identification test:
It was achievable to determine that amoxicillin was being used via the utilisation of a chemical test that focused on primary aromatic amines. When about 2 milligrammes of the drug are dissolved in 2 millilitres of water, the resulting solution will induce the action with primary amines (IP).

Solubility:
The absorption of Amoxicillin was investigated in two different solvents: water and alcohol.

Concept of Co- Concept of Co-micronization in micronization in Formulation of Rapid Dispersible ispersible Tablets:
Orodispersible tablets, also known as tablets that dissolve fast, disintegrate quickly, or dissolve in the mouth, have been the focus of an increasing amount of research over the last several years. In recent years, these dosage forms have seen increased appeal as a result of the distinctive qualities and advantages they have over more traditional forms of dose administration. After being taken, these fast dispersible tablets not only have the potential to spread out quickly but also to immediately release their active ingredients. In addition to these two benefits, these tablets also have a wonderful flavour. Reformulated pharmaceuticals make use of a wide variety of modern manufacturing techniques, including, but not limited to, solid dispersion, particle size reduction, micronization, direct compaction, melt granulation, and solvent deposition inclusion. During the production process for the drug, complexation processes were used in several ways. Finding a way to rapidly give medications that aren't especially water-soluble has been the primary motivation behind the majority of these recent scientific advances. Poor pharmacokinetics are responsible for the failure of the majority of clinical studies, which is why more than one-third of all drugs now in development are water-insoluble.Cefixime is a component of this as well. The fact that cefixime does not dissolve in water is cefixime's most significant downside. The first available form of cefixime was in the form of hard gelatin capsules. This was presumably because it was difficult to create a tablet that was a fair size and swiftly broke down the active ingredient in a compressed dosage form that was a good size and easy for patients to swallow at the time. This problem was probably the cause of this situation. There are a number of different methods in which the release schedule for cefixime may be modified. In the scientific literature and in patents, many approaches, including solid dispersion, lowering the size of cefixime, and others, have been considered. In 2007, Pia Thybo and her colleagues were doing research on tolfenamide when they made the discovery that they could make it stable and have it be extremely bioavailable. Pia Thybo and her colleagues pioneered the development of cefixime and polyvinylpyrrolidone K-30 solid dispersions (SDs) in the year 2007. Because cefixime was notoriously difficult to dissolve, they were added to the formula in order to hasten the process (PVP). The solid

tolfenamic acid mixture that he tested on animals was produced by him via the use of a procedure called spray drying. Experiments performed on the formulation that included dissolving showed the release profile of cefixime increased in every solid dispersion formulation that was tested. Because of the increased concentration of PVP in the solid dispersion, cefixime did not undergo any phase transitions over the course of the examination of its stability. In 1982, Raunio and his colleagues improved the solubility of cefixime by adding surfactants to their research. When more Brij and polysorbate 80 were added to an aqueous solution, cefixime exhibited an increased degree of solubility. The quantity of soluble rose in tandem with the number of surfactant molecules that are incompatible with water. The use of the surfactant Brij 58 within the mixture contributed to the formulation producing the most favourable release profile. In the year 2000, Gebhard and colleagues developed a fast-acting form of cefixime by using a technique known as "micronization," which decreases the size of the individual particles. In light of his results, it is probable that micronizing tolfenamic acid would lead to a more uniform release profile and an improvement in the bioavailability of cefixime. This would be the consequence of the combination of the two factors. Cefixime with an average particle size of 8 microns was coupled with alginic acid and superdisintegrants such as sodium starch glycolate to get the results he sought. Co- micronizing active ingredients with certain excipients may increase the solubility of active ingredients that don't mix well in water.
Colin A. looked into the possibility of combining the micronization of ketoprofen with the necessary excipients. He made use of Precelly-24 and steel beads in order to hasten the process of disintegration. The comicronization process, which did not affect any of the many different forms of ketoprofen in any way, considerably aided in the breakdown of ketoprofen and made it much easier to do so. Spence For instance, JK and his coworkers use the same methods in order to improve the CI-1040's solubility and bioavailability. The use of appropriate diluents such as microcrystalline cellulose has the potential to lessen the electrostatic contact that exists between diluents and active particles, which is a favourable conclusion of his research findings. When the particle size is reduced by the process of micronization, the electrostatic and Vander Waals interactions that occur between the particles become more powerful. The release profile of CI-1040 has also been improved as a direct consequence of the co-micronization process. According to B. Idzior-Walus et alresearch, .'s co-micronized fenofibrate has been demonstrated to impact lipid levels as well as insulin sensitivity in individuals who suffer from dyslipidemia and polymetabolic syndromes X. (2000). It has been discovered that the majority of formulations are based on making cefixime more soluble by using solid dispersion, reducing the size of the particles, and building drug complexes with betacyclodextrin. Cefixime is a nonsteroidal anti- inflammatory drug (NSAID) that can be taken orally or intravenously. It is a medication that belongs to the fenamate class of drugs. Because cefixime is not very water-soluble, the stage of absorption in which it is broken down is the one in which it is absorbed the most slowly. Reduce the particle size of an active substance in order to hasten the pace at which it is released. The goal of this research was to investigate the effects of an initial dose of cefixime consisting of 100 mg (the recommended daily dosage is between 100 and 200 mg). Co- micronization techniques have been adopted because they allow for more efficient distribution of cefixime throughout the body. When a drug has an active ingredient that doesn't dissolve very well in water, co-micronizing the medicine with diluents may be able to provide a better release profile for the medicine. Examining the effects of active micronization, active co-micronization, appropriate diluents with and without surfactants, and active co-micronization was a new technique that was developed in order to enhance the solubility and release profile of tolfenamic acid. This unique strategy was successful. These several methods were all integrated into one. Wet granulation was used in the production of tablets of tolfenamic acid so that they could be readily broken up into smaller pieces. Multiple precompression and postcompression

tests were performed on quick-dissolving tablets. The results of these tests are shown below.

Manufacturing of Rapid dispersible Tablets and its Evaluation:
The researchers had high hopes that the co-micronization method would facilitate an increase in the release of cefixime. The tablets were given disintegrants in order to facilitate their spreading out and becoming wet; nevertheless, the pace at which the tablets disintegrated was unaffected by the little quantity of disintegrants that was used. In order to successfully manufacture the recipe, it was necessary to make use of the flavouring as well as the sweetener. The particulars of the process through which the formulation was developed are outlined in Table 4.5. A simplified flowchart of an experiment's numerous phases is shown in Figure 4.1. These steps are presented in chronological order.

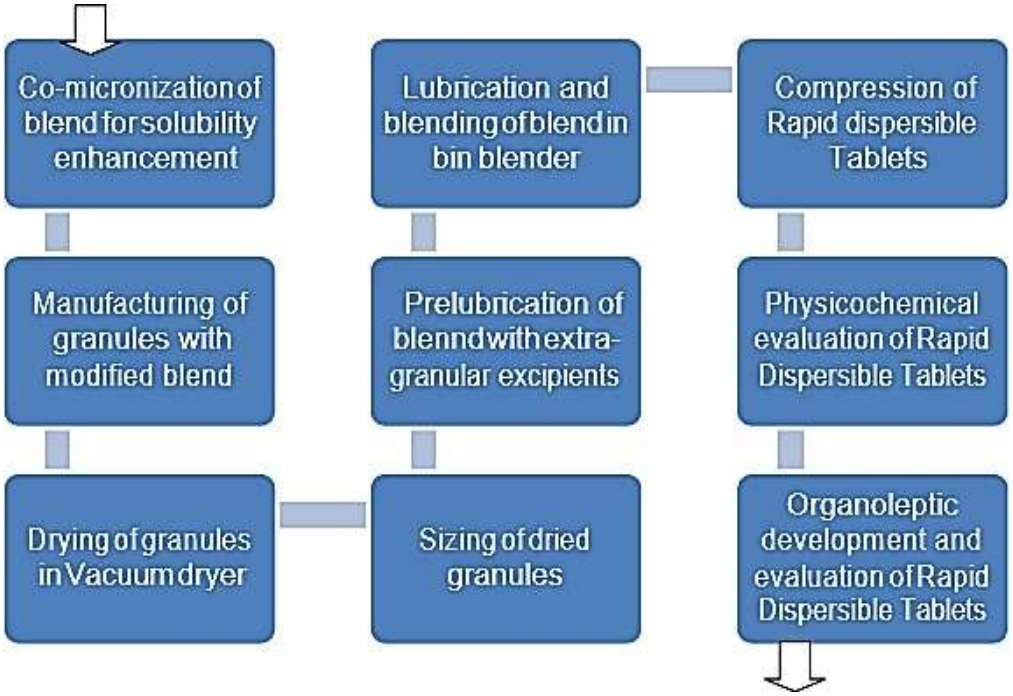


Figure. Flow Chart Describing the Experimental Procedure

Manufacturing of Co-micronization Blend:
With the use of an air-jet mill, the CE and diluents were reduced to an extremely fine powder. Co-micronization was performed on the formulation in line with the directions provided in the table. In order to guarantee that the particles were of the desired dimensions, the micronization process was repeated a total of three times. It is important to note that the formulation F-1 was not micronized; rather, it served the primary purpose of illustrating the difference between the performance of micronization and co-coating. On the other hand, formulation F-1 made use of a mesh size of sixty to make certain that cefixime was evenly dispersed throughout the combination. After undergoing further processing, the co- micronized blends were reduced to a fine powder, which was then used in the granulation process for the formulations. See Table 4.6 if you want to be prepared for co-micronization.

Table. Formulation Details of Rapid Dispersible Tablets of Cefixime

Ingredients	**Quantity available in each tablet (mg/tabs)**			
	F-1	**F-2**	**F-3**	**F-4**
Intra-granular				
Cefixime	100.00	100.00	100.00	100.00
Microcrystalline Cellulose	80.000	80.000	81.250	80.000
Sodium Lauryl Sulfate	1.250	1.250	--	1.250
Povidone (PVP K-30)	2.500	2.500	2.500	2.500
Purified Water	QS	QS	QS	QS
Extra-granular				
Mannitol	45.000	45.000	45.000	45.000
Sodium Starch Glycolate	2.500	2.500	2.500	2.500
Magnesium Stearate	1.250	1.250	1.250	1.250
Aspartame	5.000	5.000	5.000	5.000
Flavor Vanilla	2.500	2.500	2.500	2.500
Tablet Weight in mg	**240.00**	**240.00**	**240.00**	**240.00**

Table. Preparation of Co-micronization Blend for Solubility Enhancement

Formulation	**F-1**	**F-2**	**F-3**	**F-4**
Processing	Simple mixing of unmicronized CE with MCC and SLS for reference	Micronization of CE and mixing with MCC and SLS	Co-micronization of CE and MCC.	Co-micronization of CE, with MCC & SLS.

Manufacturing of Granules and Tablets:

The major objective of the study was to determine whether or not it was possible to create a fixed-dose combination of cefixime and amoxicillin. Granules of cefixime and amoxicillin were manufactured using one of two distinct granulations, and the manufacturing process for each of these granules was relatively distinct from the other. In order to get cefixime ready for the production process, the co-micronization technique was put to use. For the purpose of manufacture of amoxicillin granules for use in the pharmaceutical business, the procedures of solid dispersion and wet granulation were applied. Changing the release profile of the active ingredient in order to improve the formulation's speed of action was the primary objective of utilising cutting-edge technologies in the process of developing a fixed-dose combination of cefixime and amoxicillin.

This goal was accomplished by combining the two drugs in a single pill. Earlier development investigations have resulted in the completion of the preliminary development and optimization of individual formulations of both Cefixime and Amoxicillin dispersible tablets.

Table. Formulation details of Cefixime and Amoxicillin Tablets.

Ingredients/ Formulation Code	**Quantity in each tablet (mg/tabs)**			
	F-1	**F-2**	**F-3**	**F-4**
Part – 1 Cefixime Granules				
Cefixime	100.00	100.00	100.00	100.00
Microcrystalline Cellulose	50.00	50.00	50.00	50.00
Sodium Lauryl Sulfate	1.25	1.25	1.25	1.25
Povidone (PVP K-30)	2.50	2.50	2.50	2.50
Purified Water	QS	QS	QS	QS
Part – II Amoxicillin Granules				
Amoxicillin	125.00	125.00	125.00	125.00
Mannitol	125.00	125.00	125.00	125.00
Hypromellose	5.00	5.00	5.00	5.00
Eudragit – EPO	25.00	25.00	25.00	25.00
Polyethylene Glycol	5.00	5.00	5.00	5.00
Talc	5.00	5.00	5.00	5.00
Purified Water	QS	QS	QS	QS
Lubrication of Granules				
Ac-di-sol	25.00	--	25.00	--
Crospovidone	--	25.00	--	25.00
Aspartame	5.00	5.00	5.00	5.00
Flavor Vanilla	5.00	--	--	5.00
Flavor Strawberry	--	5.00	5.00	--
Magnesium Stearate	1.25	1.25	1.25	1.25
Tablet Weight in mg	**480.00**	**480.00**	**480.00**	**480.00**

Manufacturing of Tablet:

The compression of the granules was accomplished with the help of a Cadmach single rotating compression machine, which was also used to bring the process to a successful conclusion. In order to prevent any problems associated with sticking during the compression process, Caplet Shape extra durability punching tools with dimensions of 15.50 x 7.30 mm were employed. The average speed of the turret was kept within a regulated range of 10 to 12 revolutions per minute while the compression was taking place. In the first stages of testing, we came across several issues with the process of tabletting the grains, which included uncontrolled moisture absorption. When pills are being compressed, the humidity of the pelleting zone is monitored and recorded for accuracy. The process of tabletting could only be completed at the greatest conceivable degree of relative humidity, which was at a level of fifty percent relative humidity.

Figure. IR Spectra of Amoxicillin

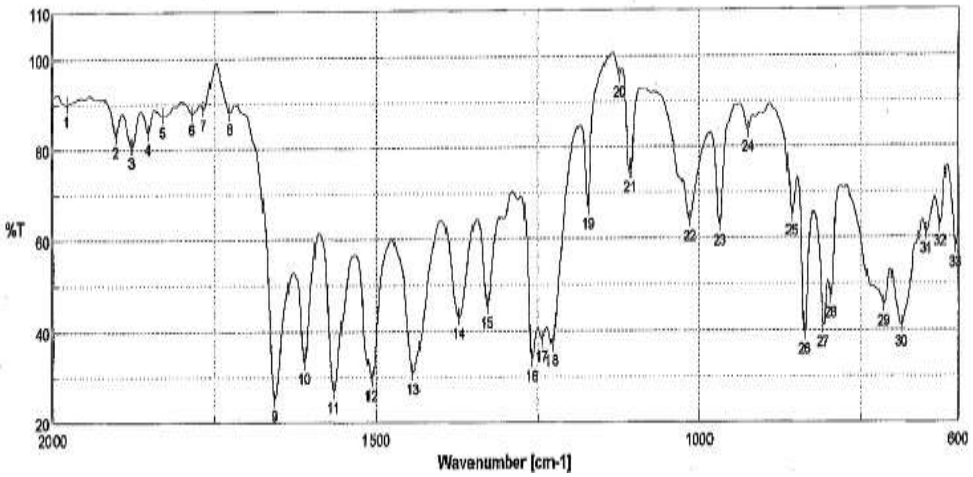


Figure .IR Spectra of Cefixime

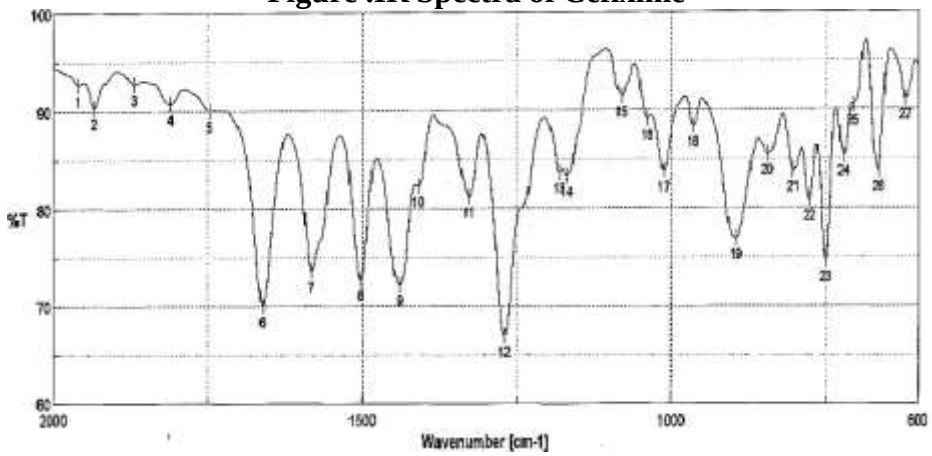


Figure. Calibration Curve of Amoxicillin

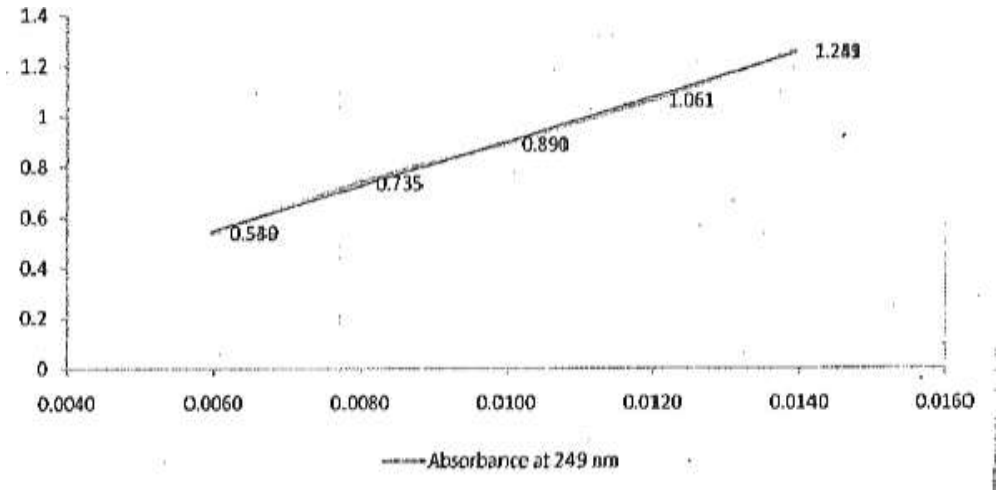
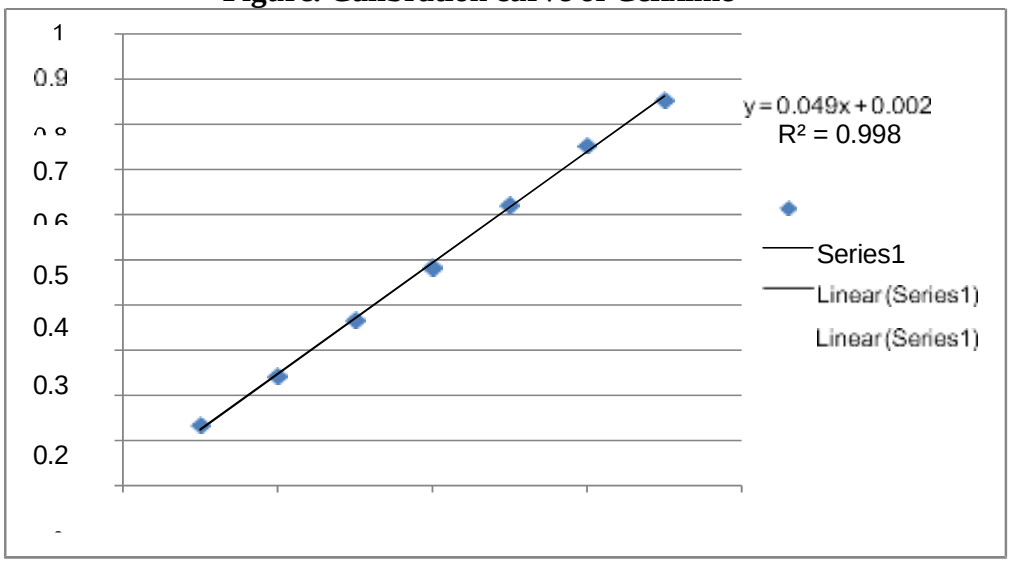


Figure. Calibration curve of Cefixime

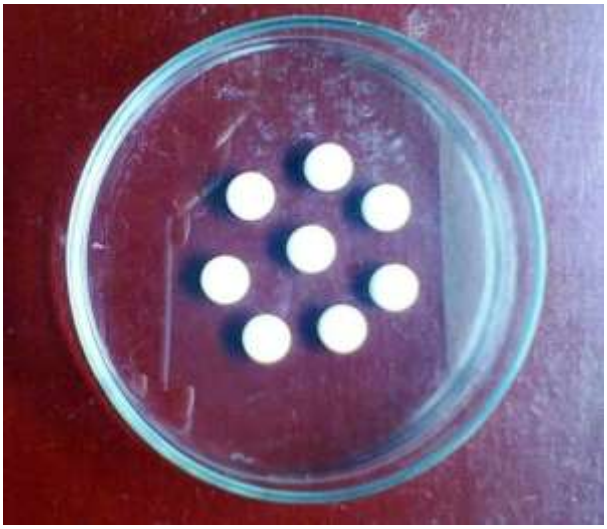


Physical Evaluation of Tablets:

Evaluation Parameters	**F-1**	**F-2**	**F-3**	**F-4**
Appearance	Off-white colored, 9.0± 0.1 mm, round flat faced tablet			
Weight Variation (%)	241.56± 2.35	241.34± 1.93	241.01± 2.46	240.85± 2.29
Hardness (Newton) n=6	28.67± 2.50	30.00± 2.10	33.33± 2.16	35.00± 1.26
Thickness (mm) n=6	3.20± 0.01	3.18± 0.02	3.20± 0.02	3.19± 0.02
Friability (% w/w)	0.65	0.68	0.72	0.69
Disintegration (Seconds)	15 – 20	18 – 22	15 – 20	17– 22

Dispersion (Seconds) n=3	50.67± 1.15	43.67± 1.53	43.67± 1.00	40.00± 3.00
Wetting Time (Seconds) n=3	65.00± 3.00	55.00± 2.00	43.67± 1.53	40.00± 2.00
Water Absorption Ratio	53.17	55.79	61.82	66.08

Figure. Appearance of Cefixime Rapid Dispersible Tablets



Analytical Evaluation of Tablets:

Table. Assay of Drug Content in Tablets

Evaluation Parameters	**F-1**	**F-2**	**F-3**	**F-4**
Drug Content (%) n=3	100.97± 1.75	100.30± 1.97	100.80± 1.73	100.33± 1.63
Content Uniformity (%) n=10	Passed	Passed	Passed	Passed

Table. In-vitro Drug Release Profile

% Drug Release in minutes	**F-1**	**F-2**	**F-3**	**F-4**
5	40	55	79	82
10	55	64	84	87
15	67	76	89	92

30	80	86	94	98
45	88	92	98	98
60	96	100	102	101

The amount of medicine included in each tablet, as well as the uniformity with which it was dispensed, were all within the permissible ranges in each and every one of the formulations F-1 through F-4. There was not a discernible difference in the granulation produced by making use of co-micronization as opposed to just mixing the mixture, as was mentioned before. According to the findings, there was a correlation between the co-micronization of the formulations and the rate of drug release. Each of the four formulations, F-1 through F-4, has a rate of release into the environment that is approximately equivalent to forty percent. This indicates that within 15 minutes, the release profiles of formulations 1 through 4 should reach 67 percent to 89 percent of their maximum values. After dissolving for half an hour, there was no change that could be considered statistically significant. In every formulation, with the exception of Formulas 3 and 4, the active component was made available to the body in less than 15 minutes after dissolution. It was discovered that both the A1 and F-2 formulations instantly released around 80 percent of the drug. They were unique in comparison to the F-1 and F-2 formulations, which administered the medication at a slower rate.

REFERANCES:

1. Salunke, S, Liu, F, Batchelor, H, Walsh, J, Turner, R, Ju, TR & Tuleu, C 2017, „European Paediatric Formulation Initiative (EuPFI)- Formulating Ideas for Better Medicines for Children“, AAPS PharmSciTech, vol. 18, no. 2, pp. 257-262.
2. AAP (American Academy of Pediatrics), Committee on Drugs. Inactive ingredients in pharmaceutical products: update (subject review). Pediatrics, 1997; 99:268–78.
3. Aastha S, Srinivas N and Sravanthi M., “Formulation and In-Vitro Evaluation of Matrix Type Sustained Release Tablets of Paliperidone”, Innovations in Pharmaceuticals and Pharmacotherapy, 2013, 1 (3), 185-198.
4. Abdul H, Gopinath M, “Formulation and evaluation of Paliperidone Nanocrystals”, Bio Med Rx, 2013, 1 (5), 422-438.
5. Aboelwafa, A. A., & Fahmy, R. H. (2012). A pilot human pharmacokinetic study and influence of formulation factors on orodispersible tablet incorporating meloxicam solid dispersion using factorial design. Pharmaceutical development and technology, 17(1), 1-14.
6. Adolfsson Å , Olsson H, Nyström C. Effect of particle size and compaction load on interparticulate bonding structure for some pharmaceutical materials studied by compaction and strength characterisation in butanol. Eur J Pharm Biopharm. 1997;44(3):243–51.
7. Afaque RMA, Saddamhusen JM, Gosavi JP. Review on artificial sweeteners used in formulation of sugar free syrups. Int J Adv Pharm, 2015; 4(2):2,4.
8. Aleksovski, A., Dreu, R., Gašperlin, M., & Planinšek, O. (2015). Mini-tablets: a contemporary system for oral drug delivery in targeted patient groups. Expert opinion on drug delivery, 12(1), 65-84.
9. Amrutkar, P. P., Patil, S. B., Todarwal, A. N., Wagh, M. A., Kothawade, P. D., & Surawase,
10. R. K. (2010). Design and evaluation of taste masked chewable dispersible tablet of lamotrigine by melt granulation. International Journal of Drug Delivery, 2(2), 183-191.
11. Anil Kumar, Vikas Kaushik, Kuldeep Malodia, Sunil Kumar and Pankaj Rakha (2012): “A Recent Approach on Fast Dissolving Tablets”, Research Journal of Pharmaceutical, Biological

and Chemical Sciences, July – September 2012, Vol 3:3, pp. 1209-1219.
12. Arima, H., Higashi, T., & Motoyama, K. (2012). Improvement of the bitter taste of drugs by complexation with cyclodextrins: applications, evaluations and mechanisms. Therapeutic delivery, 3(5), 633-644.
13. Arunachalam, A., Karthikeyan, M., Kumar, S. A., Konam, K., Prasad, P. H., Sethuraman, S., & Manidipa, S. (2010). Fast dissolving drug delivery system: A review. Journal of global trends in pharmaceutical sciences, 1(1), 92-110.
14. Arya, A., Chandra, A., Sharma, V., & Pathak, K. (2010). Fast dissolving oral films: an innovative drug delivery system and dosage form. International Journal of ChemTech Research, 2(1), 576-583.
15. Assaf, S. M., Qandil, A. M., & Al-Ani, E. A. (2013). Fast and pH-dependent release of domperidone from orally disintegrating tablets. Pharmaceutical development and technology, 18(4), 897-905.
16. Bala, R., Pawar, P., Khanna, S., & Arora, S. (2013). Orally dissolving strips: A new approach to oral drug delivery system. International journal of pharmaceutical investigation, 3(2), 67.
17. Bandari, S., Mittapalli, R. K., & Gannu, R. (2014). Orodispersible tablets: An overview. Asian Journal of Pharmaceutics (AJP): Free full text articles from Asian J Pharm, 2(1).
18. Bandari, S., Mittapalli, R. K., & Gannu, R. (2014). Orodispersible tablets: An overview. Asian Journal of Pharmaceutics (AJP): Free full text articles from Asian J Pharm, 2(1).
19. Barghi, L., & Jahangiri, A. (2018). Fast-dissolving nanofibers: As an emerging platform in pediatric and geriatric drug delivery. Journal of advanced chemical and pharmaceutical materials (JACPM), 1(2), 26-28.
20. Barghi, L., & Jahangiri, A. (2018). Fast-dissolving nanofibers: As an emerging platform in pediatric and geriatric drug delivery. Journal of advanced chemical and pharmaceutical materials (JACPM), 1(2), 26-28.
21. Bath PM, Lee HS, Everton LF (2018) Swallowing therapy for dysphagia in acute and subacute stroke. Cochrane Database Syst Rev 10: CD030032.
22. Battu, S. K., Repka, M. A., Majumdar, S., & Rao Y, M. (2007). Formulation and evaluation of rapidly disintegrating fenoverine tablets: effect of super disintegrants. Drug development and industrial pharmacy, 33(11), 1225-1232.
23. Baumann A, Katz PO (2016) Functional disorders of swallowing. Handb Clin Neurol 139: 483-488.
24. Beri, C., & Sacher, I. (2013). Development of fast disintegration tablets as oral drug delivery system-A review. Indian Journal of Pharmaceutical and Biological Research, 1(03), 80-99.
25. Bess W S, Kulkarni N, Ambike SH, Ramsay MP, (2006): "Fast dissolving orally consumable solid film containing a taste masking agent and pharmaceutically active agent at weight ratio of 1:3 to 3:1". US Patent 7067116.
26. Birer, M., & Acartürk, F. (2021). Electrospun orally disintegrating film formulation of telmisartan. Pharmaceutical Development and Technology, 26(6), 661-672.
27. Boateng, J. (2017). Drug delivery innovations to address global health challenges for pediatric and geriatric populations (through improvements in patient compliance). Journal of Pharmaceutical Sciences, 106(11), 3188-3198.
28. Bolhuis GK, Kamp HV and Lerk CF (1986). On the similarity of sodium starch glycolate from different sources. Drug Dev Ind Pharm 12: 621-630.
29. Breitkreutz, J., & Boos, J. (2007). Paediatric and geriatric drug delivery. Expert opinion on drug delivery, 4(1), 37-45.
30. Brooks M, McLaughlin E, Shields N (2019) expiratory muscle strength training improves

swallowing and respiratory outcomes in people with dysphagia: A systematic review. Int J Speech Lang Pathol 21: 89-100.
31. Brown, D. (2003). Orally disintegrating tablets-taste over speed. Drug Delivery Technol., 3, 58-61.
32. Chandrasekaran P. and R. Kandasamy, Solid oral flexible formulations for paediatric andgeriatric patients: age-appropriate formulation platforms, Indian J. Pharm. Sci.2018; 80(1):14-25.
33. Chandrasekaran, G., & Rajalakshmi, A. N. (2019). Fixed dose combination products as Oro-dispersible tablets: A review. Journal of Drug Delivery and Therapeutics, 9(2), 563-573.
34. Channer, K. S. & Virgee, J. P., (1986): "The effect of size and shape of tablets on their esophageal transit". J. Clin. Pharmac. 26: pp. 141-146.
35. Charoo, N. A., Shamsher, A. A., Zidan, A. S., & Rahman, Z. (2012). Quality by design approach for formulation development: a case study of dispersible tablets. International journal of pharmaceutics, 423(2), 167-178.
36. Chein, Y. W. (1992). Novel drug delivery systems. Marcel jekker Inc., New York, 13.
37. Chen, Y. D., Liang, Z. Y., Cen, Y. Y., Zhang, H., Han, M. G., Tian, Y. Q., ... & Yang, D. S. (2015). Development of oral dispersible tablets containing prednisolone nanoparticles for the management of pediatric asthma. Drug design, development and therapy, 9, 5815. `
38. Chowdary, K. R., & Hymavathi, R. (2000). Formulation and dissolution rate studies on dispersible tablets of ibuprofen. Indian journal of pharmaceutical sciences, 62(3), 213.
39. Ciavarella, A. B., Khan, M. A., Gupta, A., & Faustino, P. J. (2016). Dose uniformity of scored and unscored tablets: Application of the FDA Tablet Scoring Guidance for Industry. PDA journal of pharmaceutical science and technology, 70(6), 523-532.
40. Cohen, R., de La Rocque, F., Lécuyer, A., Wollner, C., Bodin, M. J., & Wollner, A. (2009). Study of the acceptability of antibiotic syrups, suspensions, and oral solutions prescribed to pediatric outpatients. European journal of pediatrics, 168(7), 851-857.
41. Cram A., J. Breitkreutz, S. Desset-Brèthes, T. Nunn, C. Tuleu, Challenges of developingpalatable oral paediatric formulations, Int. J. Pharm. 2009; (365):1-3 http://dx.doi.org/10.1016/j.ijpharm.2008.09.015
42. Cuzzolin, L., Atzei, A., & Fanos, V. (2006). Off-label and unlicensed prescribing for newborns and children in different settings: a review of the literature and a consideration about drug safety. Expert opinion on drug safety, 5(5), 703-718.
43. Deepak K., (2004): "Orally disintegrating tablets". J. Tablets and Capsules, 2004; 7: pp. 30- 35.
44. Drumond, N., van Riet-Nales, D. A., Karapinar-Çarkit, F., & Stegemann, S. (2017). Patients" appropriateness, acceptability, usability and preferences for pharmaceutical preparations: Results from a literature review on clinical evidence. International journal of pharmaceutics, 521(1-2), 294-305.
45. Dutta S and Kumar P. (2011): International Journal Drug Formulation and Research; 2(1): pp. 45-51.
46. EMA (European Medicines Agency). Reflection paper: formulations of choice for the pediatric population (CHMP). Committee for Medicinal Products for Human Use, 3, p 22, 2006.
47. Ernest T., Challenges associated with developing medicines for children-an industryPerspective, EuPFI presentation [Accessed on 12 Dec 2016]
48. ESSD (2012) position Statements: Oropharyngeal dysphagia in adult patients. European Society for Swallowing Disorders.
49. European Medicines Agency 1994, ICH Topic E7, „Note for Guidance for studies in support of Special Populations", Geriatrics.
50. European Medicines Agency 2013, „Guideline on the pharmaceutical development of medicines for paediatric use".

51. FDA 2001, Guidance for Industry, „Content and Format for Geriatric Labeling", Center for Drug Evaluation and Research (CDER), Center for Biologics Evaluation and Research (CBER).
52. FDA 2016. Guidance for Industry, „Pharmacy Compounding of Human Drug Products Under Section 503A of the Federal Food, Drug, and Cosmetic Act", Food and Drug Administration, Center of Drug Evaluation and Research (CDER), Compounding and Related Documents.
53. Fiocchi A, Riva E, Giovannini M. Ethanol in medicines and other products intended for children. Nutr Res, 1999; 19(3):373–9.