EDUZONE: International Peer Reviewed/Refereed Multidisciplinary Journal (EIPRMJ), ISSN: 2319-5045
Volume 13, Issue 2, July-December, 2024, Available online at: www.eduzonejournal.com

An Analysis Comparing the Gastrointestinal Transit of Two Different Formulations—Pellets and Tablet

Hamoud Salem Al-Mutairi[1], Abdullah Mohammed Alotaibi[2], Shorouq Majed Al-Mutairi[3], Sami Mubarak Al-Mutairi[4], Abdulaziz Saeed Alshahrani[5]

[1,2,4]Pharmacy Technician, Prince Sultan Military Medical City, Riyadh KSA City
[3]Pharmacy Specialist, Prince Sultan Military Medical City, Riyadh KSA
[5]Pharmacy Technician, Najran Armed Forces Hospital, KSA

ABSTRACT

The oral formulations of pellets and tablets are compared and evaluated in this study to determine how long it takes for the gastrointestinal (GI) tract to move through the body. A total of eight participants took part in the research, and each of them was given both formulations. Gastric emptying (MGET), small intestine transit (MSITT), colon transit (MCTT), and total transit time (MTTT) were the four stages at which the times of gastrointestinal transit were measured that were taken into consideration. The findings demonstrated that pellets have a significantly shorter time required for the stomach to empty (4.8 hours) in comparison to tablets (8.5 hours), which indicates that pellets are more quickly released from the stomach. On the other hand, pellets had a significantly longer colon transit time (29.5 hours) than tablets did (16.3 hours), which resulted in pellets having a longer total gastrointestinal transit time (36.2 hours) compared to tablets (27.4 hours). Despite the fact that pellets are able to pass through the colon more slowly, they are able to pass through the stomach more quickly, according to the findings that were confirmed by the analysis of individual subject data. Based on these distinct transit profiles, it appears that pellets have a higher initial absorption rate, but they may also result in a longer residence time in the gastrointestinal tract, which could potentially affect the overall effectiveness of the drug and the patient's level of comfort.

Keywords: Gastrointestinal (GI) Transit, Pellets and Tablets, Gastric Emptying (MGET), Small Intestine Transit (MSITT), Colon Transit (MCTT), Total Transit Time (MTTT), Drug Effectiveness, Patient Comfort.

INTRODUCTION

The absorption patterns of bisphosphonates, when taken orally, are highly dependent on the length of time that must pass without food (often 30 minutes) after dose. However, in reality, not all patients follow this advice, which lowers the drug's absorbed fraction and puts long-term treatment outcomes at doubt. The molecular and physical characteristics of bisphosphonates, as well as their absorption process, are associated with the crucial dependence of their activity on the postdosing fasting interval.

Since bisphosphonates are not well absorbed by the intestinal mucosa, it is likely that many of these molecules are held in the intercellular space by proteins that contain calcium. As soon as the molecules' irritating effects produce local edema, a tiny fraction of the soluble bisphosphonate molecules are able to cross the cell membrane and enter the bloodstream, marking the beginning of absorption. Low bioavailability is caused by this complex absorption pathway, and the normal digestive discomfort that patients taking oral bisphosphonates often feel is due to local irritation.

Present portion regimens depend on the comfort of discontinuously initiating this bothering component, say once week by week or when month to month rather than day to day. Then again, irregular dosing plans are related with an expanded gamble of diminished restorative reaction because of diminished retention. Consequently, for remedial viability in clinical practice, it is critical to ensure that solvent bisphosphonate particles arrive at the site of assimilation no later than 30 minutes after dose.

As of now, alendronate is the medication of decision for treating osteoporosis. Retention can happen in both the stomach and the underlying piece of the small digestive system, as per exploratory pharmacokinetic examinations. Subsequently, less side effects in the upper gastrointestinal system ought normal to go with the medication's fast conveyance to the digestive tract. In a non-aggravation, drinkable plan with a focus beneath 1%, the oral arrangement gives dissolvable alendronate. This plan evades the issues referenced with strong details, for example, the tablet adhering to the stomach related mucosa, the trouble in beating potential motility obstructions like hernias, fits, and the patient's body position during

travel, and the corrosiveness and slow, factor pace of breaking down that causes the precipitation or reflux of aggravation particles. In the event that the held alendronate doesn't come into contact with food or the high mineral substance of water during the post-dosing fasting period, it will animate retention through the gastric walls.

Drinkable details of alendronate are more advantageous for patients going through long haul treatment for osteoporosis because of the present irregular example of organization. With this foundation, we set off on a mission to look at the upper GI travel seasons of alendronate given as a tablet and a drinkable arrangement in an example of sound grown-ups. Our objective was to gather quantitative information on how the two plans varied in organization, which could impact their clinical use. As per present administrative principles, not set in stone on the off chance that the two plans were bioequivalent before our examination.

LITERATURE REVIEW

Maderuelo, C., et.al., (2019)explored into an assortment of definition methods for both solid and multiarticulate frameworks. Exploring an intestinal covering is a typical move toward the development of oral medicine measurement structures. Enzymatic breakdown and the stomach's acidic pH can hurt a few medications, but intestinal covering shields them from these issues. There is some conflict about whether intestinal covering builds the bioavailability of a few medications. The utilization of intestinal covering has been shown in various examination review to improve the bioavailability of explicit medications. Different drug oral dose structures and conveyance frameworks that coordinate intestinal covering with extra techniques to improve the bioavailability of orally regulated meds are enveloped in these examinations. Then again, the bioavailability, serum levels, and remedial impact of these medications may be affected by gastrointestinal pH esteems, the gastrointestinal climate, between or intra-individual fluctuation in gastric purging and gastrointestinal travel time, interpatient changeability connected with the kind of polymer utilized for intestinal covering, and other detailing factors. New oral measurement structures need extra review to decide what intestinal covering means for bioavailability.

Kambayashi, A., et.al., (2020)explored the impacts of feast admission and dozing propensities on the gastrointestinal travel of two particular measurement structures in people: hydrogel lattice expanded discharge (emergency room) tablets with a 9 mm breadth and pellets with a width going from 150 to 200 μm. The accompanying dosing conditions were utilized: fasting state at 8 AM or 8 PM, took care of state at similar times, and 240 mL of water were directed to hydrogel network emergency room tablets and cases containing 99mTc pellets, which were radiolabeled with (^{111}In). A calorie and fat-heavy lunch was eaten in the fed state experiments. The two dosage forms were monitored for small intestine transit and stomach emptying timings using gamma scintigraphy. Both dosage forms exhibited longer stomach emptying periods when taken with meals, but their small intestine transit times were unaffected. While the length of administration did not significantly affect small intestine transit or gastric emptying for any of the dosage forms, it did have an adverse effect on the stomach emptying of the ER pill.

Vinarov, Z., et.al., (2021)investigated the main reasons for the variation in oral drug exposure and potential remedies for these issues, highlighting the gaps in our understanding and outlining the path forward for future research in this area. The therapeutic benefits of oral medications can be negatively impacted by the large variety in their absorption. We can identify the source of variability as interindividual variability in physiology, changes in particular groups (age- and disease-dependent), peculiarities of medications and formulations, or interactions between meals and drugs. The clinical evidence about the impact of specific factors on the variability of drug pharmacokinetics is expanding. Among these variables are changes in gastric pH and emptying time, features of the fluid in the small intestine, disparities in development and age, and alterations to the gastrointestinal system caused by surgery. However, there is yet no conclusive evidence linking the determinants of medication absorption to gender differences, gut-related diseases (such as cachexia, chronic constipation, or anorexia), or colonic factors (such as transit time, fluid composition, or microbiome). There is a solution to the problem of oral drug pharmacokinetic variability that can be found in the pharmaceutical business. Clinical data shows that formulation tactics used to manufacture drugs can reduce the variability in oral exposure.

Priyanka, P., et.al., (2018)explored a new trend in solid dosage form design, researched mini-tablets aim to overcome certain therapeutic roadblocks. Because they are simpler to make and have fewer stability issues than pellets or any other oral dose form, mini tablets, which come in many unit dosage forms, are preferable. providing a few therapeutic advantages, like combination release patterns and dose flexibility. Mini tablets can be used to prevent local irritation and don't require any solvent during manufacture. Mini tablets provide with a number of benefits, including ease of manufacturing, minimal coating material requirements, and considerable formulation development flexibility. Because

they're easier to swallow, little tablets are more acceptable to older adults and youngsters. The goal of controlled medication delivery systems is to decrease the frequency of dose and boost the medicine's localized effectiveness.

Gazzaniga, A., et.al., (2022)improved pharmacological treatments with low systemic exposure and high local drug concentrations has sparked interest, especially in light of the high prevalence of inflammatory bowel disease.The rationale and principal delivery technology of the time-dependent method for oral colon delivery are given and discussed. The transportation of bioactive substances ingested orally to the colon has been the focus of pharmaceutical research for the past few decades, even though these routes have poor absorption properties. The use of colonic release for the administration of biologics that have stability and permeability issues in the gastrointestinal tract has also been studied. A number of methods have been suggested for colon delivery; one such method, time-dependent systems, depends on a small intestine transit time that is relatively constant. Medications that take use of this physiological feature have a delay that controls when they are released and lasts throughout the entire small intestine transit. Capsule plugs or functional polymer coatings are the main tools used for this. These materials work in response to aqueous fluids in a number of ways, including as swelling, dissolving or erosion, rupturing, and improved permeability. In addition, time-controlled formulations usually require enteric coating to protect them against the effects of different gastric emptying rates in the stomach.

RESEARCH METHODOLOGY

Data Collection
Each of the eight people who took part in the research study was given a combination of tablets and pellets. Total transit time (MTTT), small intestine transit (MSITT), colon transit (MCTT), and gastric emptying (MGET) were the four stages of gastrointestinal transit times that were measured. The lengths of transit for both formulations were recorded individually for each participant under carefully controlled conditions. This was done to ensure that the results were accurate and consistent.

Research Design
Due to the fact that a within-subjects design was utilized, each participant had the opportunity to serve as their own control. This method enabled a direct comparison of the transit lengths for tablets and pellets, which consequently minimized the subject variability that was present. In order to take into consideration, the impact of external factors on digestion, measurements were carried out in a controlled environment.

Data Analysis
Following the completion of the analysis of the data that was received, the mean and standard deviation values for each step and formulation were determined. Using 95% confidence intervals, the statistical significance of the differences between pellets and tablets was evaluated. The results of the investigation showed that, in comparison to tablets, pellets had a much faster stomach emptying time but a longer colon transit time. This investigation offered insight on the distinct ways in which the two formulations behaved at different phases of the gastrointestinal transit during the course of the study.

Data Analysis
There are significant discrepancies between the gastrointestinal (GI) transit durations of pellets and tablets across the various stages of the digestive tract. The 95% confidence interval indicates that there is a statistically significant difference between the time it takes for tablets to empty the stomach and the time it takes for pellets to empty the stomach (4.8 hours versus 8.5 hours). It takes pellets slightly longer (4.2 hours) to pass through the small intestine than it does tablets (3.1 hours), but this difference is not statistically significant. Plasters, on the other hand, have a significantly longer colon transit time than tablets do (16.3 hours), and this difference is statistically significant. Pellets take 29.5 hours to go through the colon. Similarly, the total amount of time it takes for pellets to go from one location to another is substantially longer than that of tablets (27.4 hours). When compared to tablets, pellets are able to exit the stomach more rapidly, but they require a longer period of time to go through the colon and finish their journey through the gastrointestinal tract.

Table 1: Average (standard deviation) GI transit times (h) for the tablets and pellets, and 95% C1 for the variations in transit times between the two formulations (n = 8)

Formulation	Gastric Emptying (MGET)	Small Intestine Transit (MSITT)	Colon Transit (MCTT)	Total Transit (MTTT)
	Mean (SD) [h]	Mean (SD) [h]	Mean (SD) [h]	Mean (SD) [h]
Pellets	4.8 (1.2)	4.2 (1.4)	29.5 (14.5)	36.2 (15.6)
Tablet	8.5 (6.2)	3.1 (1.0)	16.3 (8.7)	27.4 (11.8)
95% CI	-10.8 to -1.4	-0.4 to 1.8	5.6 to 20.8	0.03 to 17.6

A comparison of the stomach emptying time (MGET) and colon transit time (CTT) for pellets and tablets is presented in Table 2(a) and Table 2(b), respectively, for a total of eight subjects. According to Table 2(a), the gastric emptying times for pellets are consistently longer than those for tablets, with differences ranging from five to ten hours.

This suggests that pellets are able to transit from the stomach more quickly than tablets. As an illustration, subject 1 demonstrates that pellets take 25 hours to empty the stomach, whereas tablets take 30 hours to do the same function. In contrast, the colon transit times shown in Table 2(b) demonstrate the reverse pattern, with pellets taking a much longer amount of time than tablets to move through the colon at the same rate.

As an illustration, the colon transit time for subject 1 is 35 hours when pellets are consumed, whereas the colon transit time for tablets is 15 hours.

This trend implies that pellets may exit the stomach more quickly than tablets, but they tend to pass through the colon more slowly than tablets do. This highlights the fact that pellets and tablets behave differently in different regions of the gastrointestinal tract.

Table 2(a): For each patient, the pellets and pill undergo gastric emptying (MGET)

Subject No	Pellets (Hours)	Tablets (Hours)
1	25	30
2	20	25
3	15	20
4	20	30
5	10	15
6	15	25
7	25	35
8	20	30

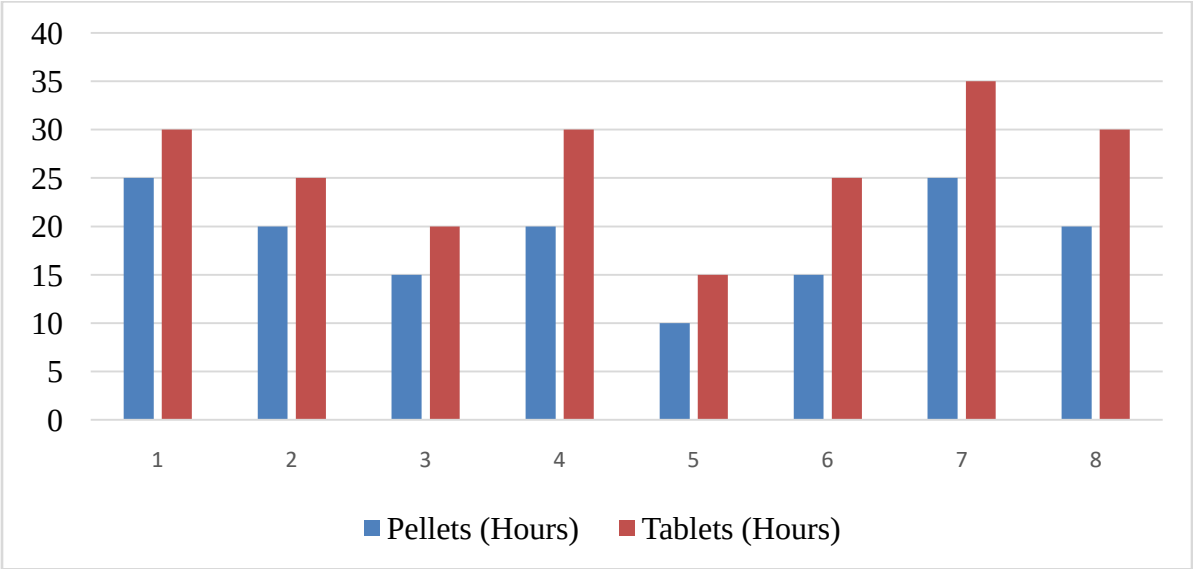

Figure1(a): For each patient, the pellets and pill undergo gastric emptying (MGET)

Table 2(b): Colon Transit (CTT): For each subject, the tablet and pellets

Subject No	Pellets (Hours)	Tablets (Hours)
1	35	15
2	20	10
3	45	30
4	40	20
5	25	15
6	30	20
7	15	10
8	35	25

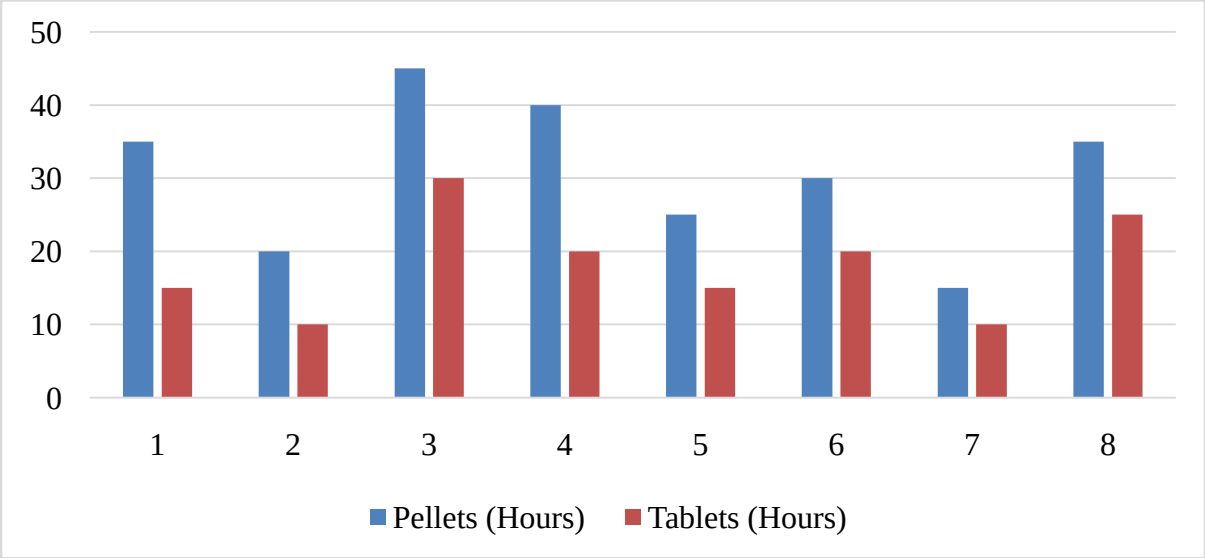

Figure1 (b): Colon Transit (CTT): For each subject, the tablet and pellets.

CONCLUSION

The results of this study show that pellets and tablets have different transit patterns in the gastrointestinal (GI) tract. Tablets take an average of 8.5 hours to empty the stomach, whereas pellets take an average of 4.8 hours. This indicates that pellets are released from the stomach faster than tablets. Pellets, on the other hand, have a substantially longer colon transit time (29.5 hours) compared to tablets (16.3 hours), which results in a longer overall gastrointestinal transit time for pellets (36.2 hours) compared to tablets (27.4 hours). Pellets are able to pass through the colon more slowly than pellets, despite the fact that they are able to clear the stomach more quickly. These findings are supported by data from individual subjects. Based on this differential performance, it appears that although pellets may assist faster initial absorption, the fact that they spend more time in the colon may have an impact on the total effectiveness of the drug as well as the patient's level of comfort.

REFERENCES

[1]. Advankar, A., Maheshwari, R., Tambe, V., Todke, P., Raval, N., Kapoor, D., & Tekade, R. K. (2019). Specialized tablets: Ancient history to modern developments. In Drug delivery systems (pp. 615-664). Academic Press.

[2]. Arnal, M. E., Denis, S., Uriot, O., Lambert, C., Holowacz, S., Paul, F., ... & Blanquet-Diot, S. (2021). Impact of oral galenic formulations of Lactobacillus salivarius on probiotic survival and interactions with microbiota in human in vitro gut models. Beneficial microbes, 12(4), 381-396.

[3]. Broesder, A., Bircan, S. Y., De Waard, A. B., Eissens, A. C., Frijlink, H. W., & Hinrichs, W. L. (2021). Formulation and in vitro evaluation of pellets containing sulfasalazine and caffeine to verify ileo-colonic drug delivery. Pharmaceutics, 13(12), 1985.
[4]. Gazzaniga, A., Moutaharrik, S., Filippin, I., Foppoli, A., Palugan, L., Maroni, A., & Cerea, M. (2022). Time-based formulation strategies for colon drug delivery. Pharmaceutics, 14(12), 2762.
[5]. Ghebre-Sellassie, I. (2022). Pellets: A general overview. Pharmaceutical pelletization technology, 1-13.
[6]. Kambayashi, A., & Kiyota, T. (2020). A physiologically-based drug absorption modeling for orally disintegrating tablets. European Journal of Pharmaceutics and Biopharmaceutics, 152, 1-9.
[7]. Kambayashi, A., Murano, M., Imai, S., Miyata, K., Sugita, K., Fujii, Y., ... & Kondo, H. (2022). Interspecies differences in gastrointestinal physiology affecting the in vivo performance of oral pharmaceutical solid dosage forms. Journal of Drug Delivery Science and Technology, 67, 102923.
[8]. Kambayashi, A., Sako, K., & Kondo, H. (2020). Effects of diurnal variation and food on gastrointestinal transit of 111In-labeled hydrogel matrix extended-release tablets and 99mTc-labeled pellets in humans. Journal of Pharmaceutical Sciences, 109(2), 1020-1025.
[9]. Maderuelo, C., Lanao, J. M., & Zarzuelo, A. (2019). Enteric coating of oral solid dosage forms as a tool to improve drug bioavailability. European Journal of Pharmaceutical Sciences, 138, 105019.
[10]. Priyanka, P., Kumar, K., & Teotia, D. (2018). A comprehensive review on pharmaceutical mini tablets. Journal of Drug Delivery and Therapeutics, 8(6), 382-390.
[11]. Ruiz-Picazo, A., Lozoya-Agullo, I., González-Álvarez, I., Bermejo, M., & González-Álvarez, M. (2021). Effect of excipients on oral absorption process according to the different gastrointestinal segments. Expert Opinion on Drug Delivery, 18(8), 1005-1024.
[12]. Schütt, M., Stamatopoulos, K., Batchelor, H. K., Simmons, M. J., & Alexiadis, A. (2021). Modelling and Simulation of the Drug Release from a Solid Dosage Form in the Human Ascending Colon: The Influence of Different Motility Patterns and Fluid Viscosities. Pharmaceutics, 13(6), 859.
[13]. Vanitha, K., Venkataswamy, M., Niharika, S., & Ramesh, A. (2018). Formulation development and evaluation of Mebeverine extended-release pellets. Asian Journal of Pharmacy and Technology, 8(2), 71-77.
[14]. Vinarov, Z., Abdallah, M., Agundez, J. A., Allegaert, K., Basit, A. W., Braeckmans, M., ... & Augustijns, P. (2021). Impact of gastrointestinal tract variability on oral drug absorption and pharmacokinetics: An UNGAP review. European Journal of Pharmaceutical Sciences, 162, 105812.
[15]. Wang, S., Wen, H., Li, P., Cui, M., Sun, W., Wang, H., ... & Yang, X. (2019). Formulation and evaluation of gastric-floating controlled release tablets of Ginkgolides. Journal of Drug Delivery Science and Technology, 51, 7-17.