UDC 615.4
DOI: 10.15587/2519-4852.2024.310813

MICROENCAPSULATION FOR THE DELIVERY OF TERAZOSIN HYDROCHLORIDE: DESIGN, DEVELOPMENT, AND CHARACTERIZATION

Asmaa Abdelaziz Mohamed, Hiba Ezzat Hamed, Mustafa AL-Mishlab

The aim of the work. *Terazosin HCL, which is a selective alpha-1 antagonist, has been recommended for the treatment of benign prostatic hyperplasia-related medical conditions, including hypertension and urinary tract disorders. The purpose of this research was to create microparticles that would have a prolonged release of terazosin hydrochloride (TZ). However, TZ is a medicine that is readily soluble and has a high capability of dissolving in water.*

Materials and methods. *A validated HPLC method was established to assess TZ. The TZ microparticles were produced using the process of melt dispersion by utilising cetyl palmitate (CP), myristic acid (MA), Glycerol monostearate 4055 (type II) or Kolliwax® GMS II (GMS), polyethylene glycol 400 (PEG 400) as a plasticizer, and tween 80 as a stabilizing agent. Different formulations of TZ microparticles were evaluated with regard to particle size, zeta potential, and release, and morphological scanning was performed.*

Results. *A zeta potential that falls between –22.9 and –29.4 mV is possessed by TZ microparticles. Furthermore, the size of TZ microparticles falls between 2.11 and 5.60 µm, and the polydispersity index (PDI) was between 0.24 to 0.41. In addition, the formula (F4) that included CP, GMS, PEG 400, and Tween 80 in the proportions of 0.8:0.2:1:0.5 had the highest zeta potential (ZP) and dissolved more than 85 % of TZ after 8 hours. Therefore, F4 was chosen for the purpose of conducting morphological research.*

Conclusion. *Employing the use of CP, GMS, PEG 400, and Tween 80 in a ratio of 0.8:0.2:1:0.5 could result in the generation of microparticles of TZ that are the most acceptable*

Keywords: *Terazosin, sustained release, microparticles, HPLC method, Validation, Kolliwax, Zeta potential*

How to cite:
Mohamed, A. A., Hamed, H. E., AL-Mishlab, M. (2024). Microencapsulation for the delivery of terazosin hydrochloride: design, development, and characterization. ScienceRise: Pharmaceutical Science, 4 (50), 53–59. http://doi.org/10.15587/2519-4852.2024.310813

1. Introduction

The technique of microencapsulation is a method that is utilised to secure sensitive and expensive compounds by enclosing them within a barrier that provides protection [1]. Through the use of this barrier, the chemicals can be released in a controlled manner at specific locations, times, and under specific conditions. Recent developments in the pharmaceutical sector have demonstrated the existence of complex medication compositions that are particularly prone to auto-oxidation [2]. Spray cooling, fluidized bed coating, extrusion, freeze drying, and coacervation are just a few of the many ways that can be utilized for the process of microencapsulation [2, 3] Solid lipid microparticles (SLMs) provide controlled and specific administration of drugs within a solid lipid matrix. SLMs are stabilized by a single layer of surfactant or a combination of surfactants, which results in a reduction of particle size and enhances the ability to store them for longer periods [4, 5]. SLMs often consist of fatty acids, waxes, triglycerides, or a combination thereof. Various emulsifier classes and ratios have been utilized to stabilize SLMs, including lecithin, bile salts, non-ionic emulsifiers like copolymers, sorbitan esters, and fatty acids [6]. White, crystalline terazosin hydrochloride is water-soluble [7]. Terazosin, a selective alpha-1 antagonist, was FDA-approved in 1987 for hypertension and in 1993 for the treatment of urinary tract diseases caused by benign prostatic hyperplasia [8, 9]. Terazosin, an HCl salt, is typically found in oral capsules with 1, 2, 5, or 10 mg dosages. Due to substantial plasma concentration fluctuations by oral administration, terazosin has various side effects [10, 11], such as extreme dizziness, weakness, and orthostatic hypotension [12].

The aim of this study was to encapsulate TZ in lipid matrices to extend the duration of the release and decrease fluctuation of action to reduce side effects; our research enclosed TZ in lipid matrices. Our team has established twelve distinct formulations of TZ microparticles. These formulations were created by using lipophilic components such as CP, MA, GMS, and tween 80 as a stabilizer. An evaluation was carried out on the TZ microparticles that were created.

2. Research planning (methodology)

Among the most important parts of the research process are:

1. Developing an HPLC technique for TZ and conducting validation in compliance with international criteria to ensure accurate TZ assessment.
2. The planning of formulations of TZ formulations employing lipid materials to achieve sustained release where TZ is water soluble.
3. Characterization and assessment of the formulations.

4. The optimal formulations were chosen for morphological investigation.

3. Materials and methods

TZ (99.8 %, HPLC), PEG 400, and tween 80 were purchased from Sigma-Aldrich, UK. Kolliwax® (GMS) II was obtained from BASF, Germany. Cetyl palmitate was obtained from Croda, UK. Acetonitrile, triethylamine, and glacial acetic acid, designed for HPLC, are available from E. Merck in Darmstadt, Germany.

HPLC method. The system involves a C18 (5 µm, 25 cm×4.6 mm) and acetonitrile: water: triethylamine in the ratio 60:40:0.1 and adjusts pH to 6 by glacial acetic acid as the mobile phase as modified by [13]. TZ was assayed at 254 nm by a photodiode array detector, and 20 ul was injected.

3. 1. Validation of method

System suitability. Five injections with Waters HPLC equipment assessed a 100 % standard solution's suitability.

Linearity. Terazosin HCL was assessed at 20–80 µg/ml concentrations. Slope, y-intercept, and correlation coefficient (R^2) were assessed. Furthermore, linearity is the ability to produce effects proportional to magnitude or intensity. A graph compared average area and strength. The variables are strongly correlated if $R^2>0.98$.

Accuracy. Accuracy measures how closely anticipated values match observed values. The calculation calculated the recovery percentage (*R* %) for TZ at doses of 40, 50, and 60 µg/ml. The average recovery should be 90–100 %.

Precision. HPLC was tested for intermediate TZ measurement accuracy and consistency. The repeatability was determined by six test concentration investigations. To demonstrate intermediate precision, three analyzers measured six samples with 100 % concentrations and determined the relative standard deviation (%RSD). A test's precision is assessed by how well several duplicate analyses over three days yield consistent results. Six samples with varying concentrations were tested numerous times in one day to verify accuracy. The inter-day accuracy was determined by assessing six replicate concentrations over three days.

Specificity. Specificity showed the capacity to discern primary peaks from similar peaks and the placebo. To rule out interference, specificity was measured.

Limits of detection and quantification. The limit of detection (LOD) is the lowest drug concentration or intensity that can be identified, even if mismeasured. However, the limit of quantification (LOQ) is the lowest substance concentration that can be properly quantified. LOD and LOQ were determined using the methods $\text{LOD}=3.3\times SD/S$ and $\text{LOQ}=10\times SD/S$, *SD* denotes the standard deviation, while *S* symbolizes the slope

Robustness. Being robust means that it can continue to function reliably even when subjected to little modifications. Variations in wavelength and flow rate were part of the robustness assessment.

Stress-induced degradation. A 50 µg/ml concentration was used for a stressed degradation investigation. Base hydrolysis was performed by putting 5 ml of 1 M solution at 70 °C for 1 hour. For acid hydrolysis, 5 cc of 1 M hydrochloric acid was used at 70 °C for around 1 hour. 0.5 cc of 50 % H2O2 was left for 60 minutes to degrade oxidatively. Leaving the standard solution under UV lamps generating 254 nm light for 24 h.

Microparticles preparation. The microparticles of TZ were generated by accurately weighing the stabilizer (Tween 80), which was then placed in a beaker with 100 ml of water containing PEG 400. The mixture was agitated on a thermostated mechanical shaker at a temperature of 90°. Next, (Cetyl palmitate/Myristic acid) was introduced and agitated until it melted. One gram of TZ was dissolved in 25 milliliters of acetone. Subsequently, this solution was gradually introduced into a blend of liquefied lipid substances while agitating at 20,000 revolutions per minute for 20 minutes, utilizing a magnetic stirrer equipped with a heated surface. Dispersed microparticles were solidified with cold water. A vacuum pump filtered the dispersion to capture microparticles, followed by rinsing and drying in a desiccator for 48 h. A Malvern Mastersizer 2000 (Malvern UK) laser diffraction device was used to evaluate the volumetric size distributions. The TZ microparticle compositions are disclosed in Table 1.

Table 1

Formulation of microparticles

Formula	Cetyl palmitate (g)	Myristic acid (g)	GMS (g)	PEG 400 (g)	Tween 80 (g)
F1	0.2	–	0.1	1	0.5
F2	0.4	–	0.1	1	0.5
F3	0.6	–	0.2	1	0.5
F4	0.8	–	0.2	1	0.5
F5	1	–	0.5	1	0.5
F6	0.2	0.25	–	1	1
F7	0.4	0.5	–	1	1
F8	0.8	1	–	1	1
F9	1	1	–	1	1
F10	–	0.5	0.1	1	1
F11	–	1	0.2	1	0.5
F12	–	1	0.2	1	0.5

3. 2. TZ microparticles characterization

Encapsulation efficiency (EE).

Centrifugation technique was employed to calculate EE of TZ. Microparticles (including TZ equivalent to 10 mg) were dispersed and centrifuged at 20000 rpm for 30 min in a refrigerated centrifuge to obtain the supernatant. Then, the concentrated liquid was filtered to determine the free TZ concentration after dilution and analyzed. The following equation was employed [14–16]:

$$\%EE=\frac{\text{weight of drug incorporated}\times 100}{\text{weight of drug initialy taken}}.$$

Particle size and surface charge.

Using a Zetasizer equipment manufactured by Malvern Instruments, UK, we assessed the stability and distribution of TZ microparticles using photon correlation spectroscopy. Each sample was subjected to three determinations following adequate dilution with filtered deionized water, and the findings were reported as mean values.

In vitro drug release studies.

The microparticle powder, equivalent to 10 mg of TZ, was dissolved by passing it across a dialysis membrane with a mass cut-off of 12 KDa [17]. As a result, the bags were upheld and positioned in the basket USP dissolving testing apparatus, rotating at a speed of 50 revolutions per minute in 900 milliliters of water [18]. We transfer 5 ml samples at regular intervals of 1, 2, 4, 6, 8, 10, and 12 hours. These samples were then replaced with fresh medium to maintain a constant concentration. The percentage of TZ released from the microparticles was then calculated.

Scanning electron microscopy (SEM).

Using SEM, the surface morphology of TZ microparticles was observed. The selected TZ microparticles were gold-coated using a Baltec SCD 005 Spater coater apparatus. The micrographs are captured with a SEM-Jeol JSM 6460LV instrument.

Statistical investigation.

Utilizing the GraphPad Prism® software, we were able to determine residual SD, LOD, and LOQ.

3. Results

An HPLC technique was developed to quantify TZ, and validation characteristics were conducted according to the guidelines of ICH Q2 and USP 43 [18, 19]. The suitability features were evaluated, including the tailing factor (*T*), capacity factor (*k*'), and count of plates [19–21]. The *T*, *k*', and plate count to be 0.63, 6.2, and 6400 revealed in Table 2. The peak observed in Fig. 1, with a retention time of 8.3 min, corresponds to TZ. The peak observed in Fig. 2, with a retention time, corresponds to TZ and exhibits minimal tailing, which is less than 2, and excellent symmetry.

A calibration curve was constructed, with the Y-axis representing the peak area in microvolts (uV) and the X-axis representing microgram concentration per milliliter. The obtained R^2 is 0.9991, which falls within the specified constraints of not being less than 0.99 revealed in Fig. 1, and the recovery varied between 99.8 % and 101 %, which falls within the specified constraints shown in Table 2. Furthermore, the approach demonstrated precision as the assessments of the identical sample were comparable, with RSD values of less than 1 % or falling below the threshold of less than 2 %. Furthermore, sensitivity was underscored through the determination of the LOD) and LOQ for TZ, which were 6.3 and 19.1 µg/ml, respectively, represented in Table 2. Degradation of TZ was 5.3 %, 11.7 %, 18.6 %, and 2 % under acidic, basic, oxidation and light, respectively, indicating stability indicating characteristics of the method. Furthermore, the RSD was less than 0.4, with minor changes in the analysis conditions confirming robustness.

The TZ content exhibited a range of 89.6 % to 94.8 %, while the entrapment efficiency was 71.5 % to 92.17 %, as indicated in Table 3, which is considered acceptable. The average size of TZ microparticles varied between 2.11 and 5.6 µm, while the zeta potential of the TZ-loaded microparticles, which also contained CP and GMS, ranged from –22.9 to –29.4 mV and the polydispersity index (PDI) remained consistently between 0.24 and 0.41.

Fig. 3 shows that the formula microparticles (F4) had the largest release of TZ after 8 hours, with 85 % of the drug being released, while the formula microparticles (F9) had the lowest release of TZ, with only 51 % being released after 8 hours. Thus, the optimal formulation exhibited satisfactory release.

The zeta potential and size of the microparticles in formulation F4 are depicted in Fig. 4, 5, with a mean size of 4.21 µm. The formulation (F4) exhibited superior properties regarding high zeta potential therefore, F4 was chosen for SEM, where the TZ microparticles showed a spherical shape (Fig. 6).

Table 2

Validation parameters

Parameter	Criteria	TZ
Linearity	R^2≥0.98	0.9991
	Slope	107723
	Intercept	458046
	Regression equation	107723*x*–458046
System suitability	*T*<2	0.63
	Plates >2000	6400
	k'>2	6.2
Accuracy	Mean % recovery (95 % to 105 %)	99.9 %
	RSD≤2 %	0.36 %
Precision	Repeatability (RSD %≤5 %)	0.11 %
	Intermediate (RSD %≤10 %)	0.23 %
Sensitivity	LOD (µg/ml)	6.3
	LOQ (µg/ml)	19.1
Degradation	In 1 M HCl	84.7 %
	in 1 M NaOH	78.3 %
	in 10 % H_2O_2	81.4 %
	Photolytic	98 %
Robustness	RSD % at 253 nm	0.21 %
	RSD % at 255 nm	0.27 %
	RSD % at pH 6.1	0.22 %
	RSD % at pH 5.9	0.32 %

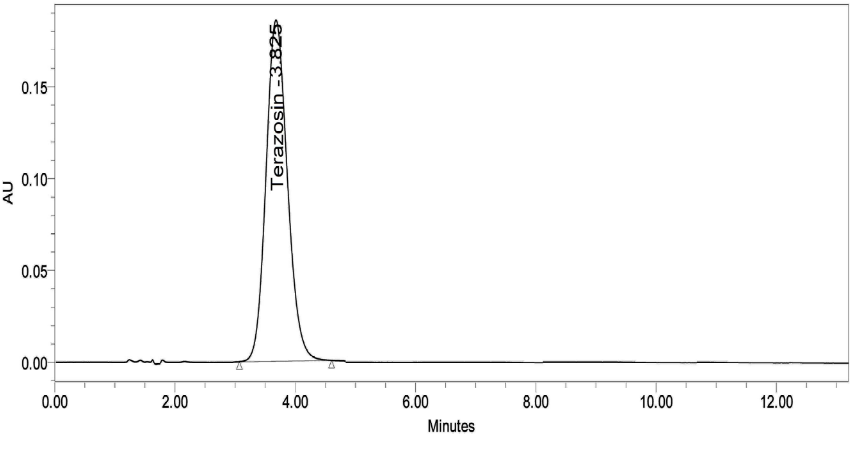

Fig. 1. Chromatogram of TZ

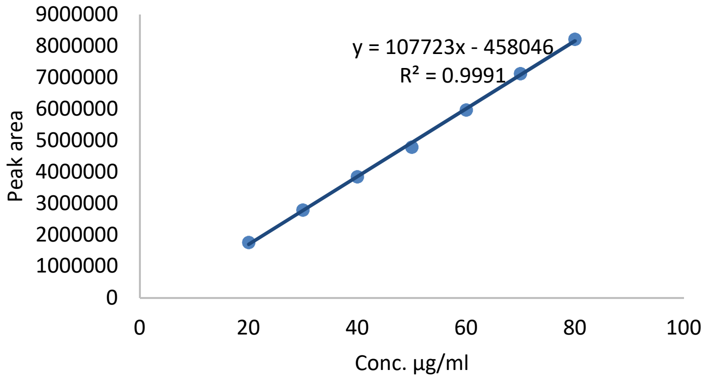

Fig. 2. Calibration curve of TZ

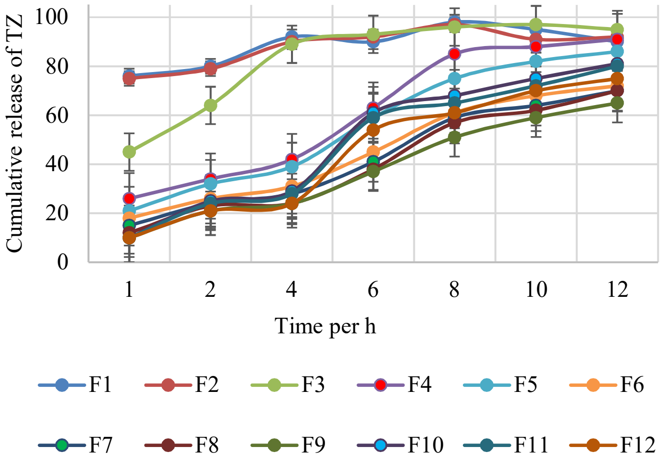

Fig 3. Dissolution of TZ microparticles

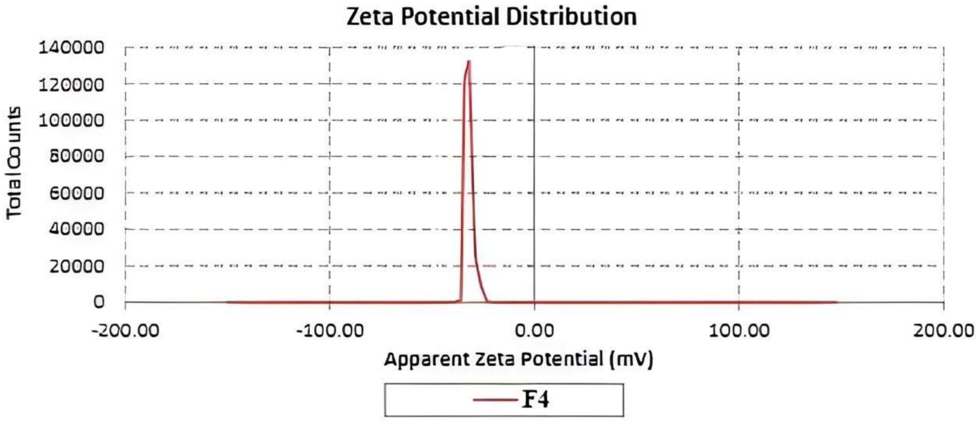

Fig 4. Zeta potential of TZ microparticles

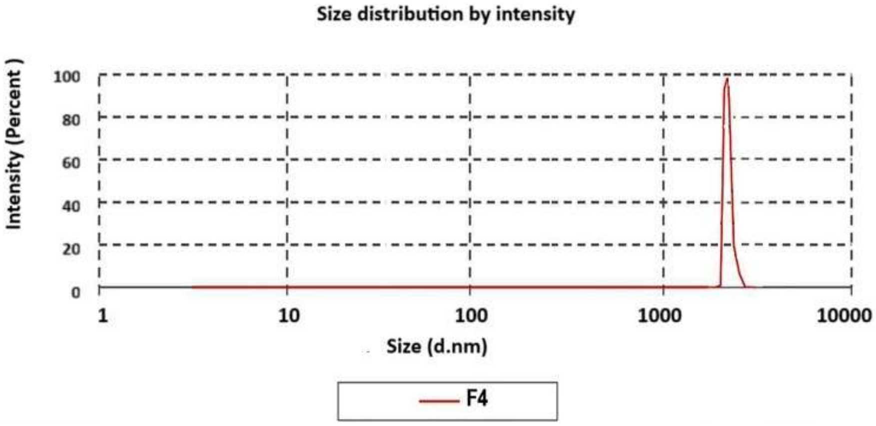

Fig. 5. Size of TZ microparticles

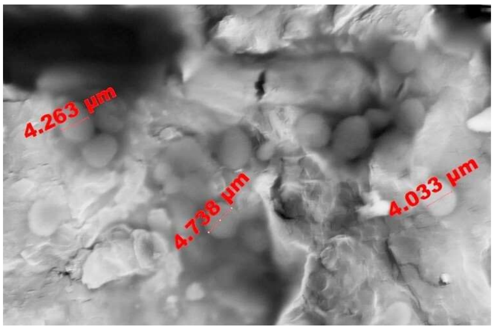

Fig. 6. SEM of F4

Table 3

Mean particle size, content, ZP and PDI

Formula	Mean drug content (%)	Mean EE (%)	ZP (mV)	Mean particle size (µm)	Mean PDI
F1	92.4	76.31	–23.1	2.56	0.40
F2	88.4	81.48	–23.6	3.48	0.39
F3	93.4	82.17	–24.6	5.27	0.37
F4	94.8	92.17	–29.4	4.21	0.24
F5	92.9	82.48	–23.4	4.14	0.29
F6	93.6	79.89	–23.6	3.64	0.38
F7	92.9	90.47	–24.1	4.24	0.27
F8	94.6	71.50	–25.6	3.59	0.39
F9	89.6	76.45	–25.9	3.49	0.41
F10	90.9	79.59	–23.2	2.11	0.37
F11	92.1	81.45	–22.9	3.49	0.27
F12	93.9	82.56	–23.4	5.60	0.36

5. Discussion

An HPLC technique was developed to quantify TZ, and validation characteristics were conducted according to the guidelines of ICH Q2 and USP 43 [17, 18]. The suitability features were evaluated, including *T*, *k*', and plate count [19, 20]. The estimates met the criteria outlined in Table 2. The peak observed in Fig. 1, with a retention time corresponds to TZ and exhibits minimal tailing which less than 2 and excellent symmetry.

Regarding the calibration curve, the obtained correlation coefficient (R^2) is 0.9991, which falls within the specified constraints of not being less than 0.99. The recovery varied between 99.8 % and 101 %. Furthermore, the approach demonstrated precision as the assessments of the identical sample were close, with relative standard deviations (RSD) of <1 % or under the threshold of <5 %. Sensitivity was highlighted by determining LOD) and LOQ for TZ, which were 6.3 and 19.1 µg/ml, respectively and the findings are depicted in Fig. 2 and Table 2.

The TZ content exhibited a range of 89.6 % to 94.8 %, while the entrapment efficiency was 71.5 % to 92.17 %, as indicated in Table 3, which is considered high. The average size of TZ microparticles varied between 2.11 and 5.6 µm, while the zeta potential of the TZ-loaded microparticles, which also contained CP and GMS, ranged from –22.9 to –29.4 mV which indicated stability of microparticles and absence of clumping was observed among the microparticles [21], and the polydispersity index (PDI) remained consistently between 0.24 and 0.41 which indicate conformity of particles size [22].

Fig. 3 shows that the formula microparticles (F4) had the largest release of TZ after 8 hours, with 85 % of the drug being released, while the formula microparticles (F9) had the lowest release of TZ, with only 51 % being released after 8 hours.

The zeta potential and size of the microparticles in formulation F4 are depicted in Fig. 4, 5, with a mean size of 4.21 µm. The liberation of TZ from (F4) exceeded 80 % after 8 hours and continued till 12 hours. In addition, the formulation (F4) exhibited superior properties regarding high zeta potential of –29.4 mV conforming stability [22] and its microencapsulation efficiency was high (92.17 %), and the sustained release of microparticles incorporating CP could be attributable to the hydrophobic characteristics of the long-chain fatty acids included in the triglyceride, which help to retain lipophilic drugs. medicines [23]. Thus, the optimal formulation F4 was chosen for SEM, where the TZ microparticles showed a spherical shape (Fig. 6). The microparticles produced may be filled in hard gelatin capsules to be employed in the pharmaceutical industry.

There is a need for more literature experiments that involve using lipid matrices to microencapsulate TZ to achieve a prolonged release. In our study, I successfully formulated loaded TZ microparticles utilizing lipid materials, marking the first attempt to include TZ in lipid matrices. Nevertheless, certain studies endeavoured to design other dosage formulations of terazosin. Kumar et al. (2014) developed sublingual TZ tablets employing several superdisintegrating agents by the direct compression technique [24]. The tablets underwent precompression and post-study evaluations. A very efficient formulation, referred to as F6, was discovered. This formulation exhibited a rapid wetting time and disintegration time, all attributed to the presence of Crosspovidone [24]. Regarding the research performed [25], TZ Fast Dissolving Tablet was prepared using superdisintegrants through direct compression and its effectiveness was evaluated [25].

Nevertheless, numerous inquiries revolve around the utilization of waxy substances. For instance, Lipid matrix controlled-release microparticles comprising azilsartan kamedoxomil (AZM) have been produced and effectively employed [17]. The AZM microparticles were synthesized by melting various waxy substances and stabilizers such as Tween 80 and Poloxamer 407. The formulations of AZM microparticles were evaluated [17]. López-Iglesias et al. developed bioactive substances SLMs containing lidocaine hydrochloride by utilizing glyceryl monostearate (GMS) [26]. The researchers then assessed the formulation's effectiveness in delivering the medicine to the site of the wound and penetrating the skin barrier. SLMs could deliver appropriate doses for pain relief and preventing infections. Furthermore, Ilyas et al. created prolonged SLMs of Bisoprolol applying waxes to improve medication pharmacokinetics and hypertensive patient compliance utilizing Carnauba and Ceresin waxes as matrices and Tween 80 [27]. Results showed that all SLMs had good micromeritics, some formulations showed controlled released.

Practical relevance. The established formulations were to extend the duration of the release, therefore, TZ was incorporated in lipid matrices. These formulations were created by using lipophilic components such as CP, MA, GMS, and tween 80 as a stabilizer and evaluation of the developed formulation was conducted chemically employing an accurate HPLC which was designed to assess TZ accurately and the selected formulation was assessed morphologically by SEM.

Limitations of the study: The current analytical method may not be utilized to calculate other medicines in combination with TZ without assessing the resolution between peaks. Furthermore, the lipophilic materials employed, such as Kollicoat, may not be appropriate for other drugs.

Prospects for further research: This study details an HPLC technique that can be employed to evaluate dosage forms containing TZ kept at elevated temperatures, serving as a stability indication assay.

6. Conclusion

Through microencapsulating TZ with lipid matrices such as cetyl palmitate, GMS, PEG 400, and stabilizer (tween 80) in the proportions of 0.8:0.2:1:0.5, it can be accomplished to produce TZ microparticles that have ideal characteristics such as a high zeta potential (–29.4 mV) confirming the stability of microparticles and the least PDI 0.24 indicating that particles are uniform. Additionally, these microparticles have a sustained release that lasts for twelve hours. The optimal formula (F4) comprised cetyl palmitate, GMS, PEG 400, and tween 80 in the ratio of 0.8:0.2:1:0.5 was assessed chemically using the developed HPLC method and morphologically by SEM. Then, it is possible to incorporate the formulation that has been optimized into capsules or tablets that have a prolonged release behaviour and are prescribed for administration.

Conflict of interests

The authors declare that they have no conflict of interest related to this research, whether financial, personal, authorship or otherwise, that could affect the research and its results revealed in this article.

Funding

The study was performed without financial support.

Data availability

Data will be made available at a reasonable request.

Use of artificial intelligence

The authors confirm they did not use artificial intelligence technologies when creating the current work.

Acknowledgements

Authors thank Alzahraa University for Women.

References

1. Choudhury, N., Meghwal, M., Das, K. (2021). Microencapsulation: An overview on concepts, methods, properties and applications in foods. Food Frontiers, 2 (4), 426–442. https://doi.org/10.1002/fft2.94

2. Gharsallaoui, A., Saurel, R., Chambin, O., Voilley, A. (2011). Pea (Pisum sativum, L.) Protein Isolate Stabilized Emulsions: A Novel System for Microencapsulation of Lipophilic Ingredients by Spray Drying. Food and Bioprocess Technology, 5 (6), 2211–2221. https://doi.org/10.1007/s11947-010-0497-z

3. Piletti, R., Zanetti, M., Jung, G., de Mello, J. M. M., Dalcanton, F., Soares, C. et al. (2019). Microencapsulation of garlic oil by β-cyclodextrin as a thermal protection method for antibacterial action. Materials Science and Engineering: C, 94, 139–149. https://doi.org/10.1016/j.msec.2018.09.037

4. Wolska, E., Brach, M. (2022). Distribution of Drug Substances in Solid Lipid Microparticles (SLM) – Methods of Analysis and Interpretation. Pharmaceutics, 14 (2), 335. https://doi.org/10.3390/pharmaceutics14020335

5. Gugu, T. H., Chime, S. A., Attama, A. A. (2015). Solid lipid microparticles: An approach for improving oral bioavailability of aspirin. Asian Journal of Pharmaceutical Sciences, 10 (5), 425–432. https://doi.org/10.1016/j.ajps.2015.06.004

6. Scalia, S., Young, P. M., Traini, D. (2014). Solid lipid microparticles as an approach to drug delivery. Expert Opinion on Drug Delivery, 12 (4), 583–599. https://doi.org/10.1517/17425247.2015.980812

7. HYTRIN (terazosin hydrochloride) Capsules (2005). FDA monograph. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2006/19057Orig1s021,%2020347Orig1s009%20lbl.pdf

8. Kumar, A., Kumar, R., Mazumdar, A. (2021). Synthesis Characterization and Antibacterial Activity of Terazosin Hydrochloride Drug and Market Formulation. Research Journal of Pharmacy and Technology, 14, 4777–4782. https://doi.org/10.52711/0974-360x.2021.00831

9. Yang, C. H., Raja, A. (2023). Terazosin. Treasure Island: StatPearls Publishing.

10. Oestreich, M. C., Vernooij, R. W., Sathianathen, N. J., Hwang, E. C., Kuntz, G. M., Koziarz, A. et al. (2020). Alpha-blockers after shock wave lithotripsy for renal or ureteral stones in adults. Cochrane Database of Systematic Reviews, 2020 (11). https://doi.org/10.1002/14651858.cd013393.pub2

11. Hundemer, G. L., Knoll, G. A., Petrcich, W., Hiremath, S., Ruzicka, M., Burns, K. D. et al. (2021). Kidney, Cardiac, and Safety Outcomes Associated With α-Blockers in Patients With CKD: A Population-Based Cohort Study. American Journal of Kidney Diseases, 77 (2), 178–189.e1. https://doi.org/10.1053/j.ajkd.2020.07.018

12. Jiang, C., Jiang, X., Wang, X., Shen, J., Zhang, M., Jiang, L. et al. (2021). Transdermal iontophoresis delivery system for terazosin hydrochloride: an in vitro and in vivo study. Drug Deliv, 28 (1), 454–462. http://dx.doi.org/10.1080/10717544.2021.1889719

13. Rudra, R., Ganguly, S., Dhua, M., Sikdar, B. (2013). Analytical Method Development & Validation for Estimation of Terazosin Hydrochloride Equivalent To Terazosin In Tablet Dosage Form. Pharmatutor. Available at: https://www.pharmatutor.org/articles/analytical-method-development-validation-estimation-terazosin-hydrochloride-equivalent-terazosin-in-tablet-dosage-form

14. Ekambaram, P., Abdul Hasan Sathali, A. (2011). Formulation and Evaluation of Solid Lipid Nanoparticles of Ramipril. Journal of Young Pharmacists, 3 (3), 216–220. https://doi.org/10.4103/0975-1483.83765

15. Eltawela, S., Abdelaziz, E., Mahmoud, M., Elghamry, H. (2021). Preparation and characterization of (−)-epigallocatechin gallate lipid based nanoparticles for enhancing availability and physical properties. Al-Azhar Journal of Pharmaceutical Sciences, 63, 17–36. http://dx.doi.org/10.21608/ajps.2021.153558

16. Castro, S. R., Ribeiro, L. N. M., Breitkreitz, M. C., Guilherme, V. A., Rodrigues da Silva, G. H., Mitsutake, H. et al. (2021). A pre-formulation study of tetracaine loaded in optimized nanostructured lipid carriers. Scientific Reports, 11 (1). https://doi.org/10.1038/s41598-021-99743-6

17. Rahi, F. A., Ameen, M. S. M., Jawad, K. K. M. (2022). Preparation and evaluation of lipid matrix microencapsulation for drug delivery of azilsartan kamedoxomil. ScienceRise: Pharmaceutical Science, 6 (40), 21–28. https://doi.org/10.15587/2519-4852.2022.270306

18. The Pharmacopoeia of United States of America", 43th Ed., National Formulary 38, Mack publishing Co. Easton, vol. 2, Electronic version (2019).

19. International Conference on Harmonization, Validation of Analytical Procedures: Text and Methodology, Q 2 (R1) (2005). ICH.

20. Sangani, M. B., Patel, N. (2024). An Eco-Friendly RP-HPLC Method Development and Validation for Quantification of Favipiravir in Bulk and Tablet Dosage Form Followed by Forced Degradation Study. Journal of Chromatographic Science, 62 (5), 432–438. https://doi.org/10.1093/chromsci/bmad093

21. Singh, N., Akhtar, M. J., Anchliya, A. (2021). Development and Validation of HPLC Method for Simultaneous Estimation of Reduced and Oxidized Glutathione in Bulk Pharmaceutical Formulation. Austin Journal of Analytical and Pharmaceutical Chemistry, 8 (1). https://doi.org/10.26420/austininternmed.2021.1129

22. Danaei, M., Dehghankhold, M., Ataei, S., Hasanzadeh Davarani, F., Javanmard, R., Dokhani, A. et al. (2018). Impact of Particle Size and Polydispersity Index on the Clinical Applications of Lipidic Nanocarrier Systems. Pharmaceutics, 10 (2), 57. https://doi.org/10.3390/pharmaceutics10020057

23. Sivadasan, D., Madavan, B., Penmatsa, S. D., Bathini, S. T. (2013). Formulation and Characterization of Solid Lipid Nanoparticles of Rifampicin. Erciyes Tıp Dergisi/Erciyes Medical Journal, 35 (1), 1–5. https://doi.org/10.5152/etd.2013.01

24. Kumar, M. K., Nagaraju, K., Bhanja, S., Sudhakar, M. (2014). Formulation and evaluation of Sublingual tablets of Terazosin hydrochloride. International Journal of Pharmaceutical Sciences and Research, 5 (2), 417–427. https://doi.org/10.13040/ijpsr.0975-8232.5(2).417-27

25. Muskan, J., Shelendra, M., Ashok, K., Sapna, M., Anil, K. (2022). Formulation and Evaluation of Fast Dissolving Tablet of Terazosin Hydrochloride. American Journal of PharmTech Research, 12, 75–87. https://doi.org/10.5281/zenodo.7407648

26. López-Iglesias, C., Quílez, C., Barros, J., Velasco, D., Alvarez-Lorenzo, C., Jorcano, J. L. et al. (2020). Lidocaine-Loaded Solid Lipid Microparticles (SLMPs) Produced from Gas-Saturated Solutions for Wound Applications. Pharmaceutics, 12 (9), 870. https://doi.org/10.3390/pharmaceutics12090870

27. Ilyas, S., Maheen, S., Andleeb, M., Khan, H. U., Shah, S., Abbas, G. et al. (2023). Development, optimization and in vitro-in vivo evaluation of solid lipid microparticles for improved pharmacokinetic profile of bisoprolol. Materials Today Communications, 37, 107097. https://doi.org/10.1016/j.mtcomm.2023.107097

Received date 17.06.2024
Accepted date 22.08.2024
Published date 30.08.2024

Asmaa Abdelaziz Mohamed, PhD of Pharmaceutics, Department of pharmaceutics, College of Pharmacy, Al-Zahraa University for Women, Karbala, Iraq

Hiba Ezzat Hamed, PhD of Pharmaceutics, Department of Pharmacy, Al-Nisour University College, Al-Nisour sq., Baghdad, Iraq

Mustafa AL-Mishlab, Master of Pharmaceutics, Department of Pharmacy, Al-Manara College for Medical Sciences, Maysan Governorate, Al-Amarah city, Iraq

***Corresponding author:** *Asmaa Abdelaziz Mohamed, e-mail: asmaa.abdelaziz@alzahraa.edu.iq*