Section A-Research paper
ISSN 2063-5346

Investigating Drug Release Kinetics from Biocompatible Guar Gum (GG)/Methyl Cellulose (MC) Blend - γ-Fe_2O_3 Nanocomposites

Prasad P.[1*], Sudhakar Y. N.[2*], Shareefraju J. Ukkund[3], Sumana V. S.[4], Shrinivasa Mayya D.[5], Savitha M. B.[6]

[*1]Project Coordinator, CISEE - Nano Technology, Srinivas Institute of Technology, Valachil, Mangaluru, D.K., Karnataka, India. Corresponding Author Email: hodnanotechsit@gmail.com

[*2]Department of Chemistry, Manipal Institute of Technology, Manipal Academy of Higher Education, Karnataka. India. Corresponding Author Email: Sudhakar.yn@manipal.edu

[3]Department of Biotechnology, PA College of Engineering, Mangaluru, D.K., Karnataka, India.

[4]Department of Chemistry, Srinivas Institute of Technology, Valachil, Mangaluru – 574143, D.K., Karnataka, India.

[5]Department of Mechanical Engineering, Srinivas Institute of Technology, Valachil, Mangaluru – 574143, D.K., Karnataka, India.

[6]Department of Chemistry and Research Centre, Sahyadri College of Engineering and Management, Adyar, Mangaluru - 575007, D.K., Karnataka, India.

DOI: 10.48047/ecb/2023.12.si4.1769

ABSTRACT

This research explores the use of water-soluble biocompatible polymers, guar gum (GG) and methyl cellulose (MC), alongside the nanomaterial maghemite (γ-Fe_2O_3), for transdermal sustained drug release, employing metoprolol succinate as a model drug. Drug-infused thin film patches of GG, MC, their γ-Fe_2O_3 nanocomposites, and 10/90 GG/MC blend - γ-Fe_2O_3 nanocomposites were utilized for the investigation. Physicochemical parameter evaluations, including thickness, weight, folding endurance, % moisture absorbance, and % moisture loss, supported the drug release kinetics study using a hydrated cellophane sheet and diffusion tube. The results indicate that this blend-nanocomposite system releases the drug through diffusion, following Fickian kinetics. These biomaterials hold promise for developing slow, sustained release formulations in transdermal drug delivery systems.

Keywords: blend-nanocomposites, guar gum, methyl cellulose, maghemite, compatibility, biocompatibility.

1. INTRODUCTION:

Researchers are increasingly focused on developing novel drugs and dosage forms to enhance efficacy while reducing side effects. Water-soluble polymers are being extensively utilized in the pharmaceutical industry [1-7]. The irregular shifts in drug concentration in the bloodstream resulting from conventional dosing have prompted the development of

controlled drug delivery systems [8, 9]. Transdermal drug release systems (TDRS) capitalize on the skin for drug administration, utilizing biocompatible polymer patches for improved absorption, patient compliance, bioavailability, and easy termination [10].

The biocompatible polymers guar gum [11-15] and methyl cellulose [16, 17], and the nanomaterial maghemite (γ-Fe_2O_3) have been commonly used in sustained drug release (DRS) applications [18, 19]. The bulging behavior of guar gum and the ability to hold water and gel forming characteristics of methyl cellulose has contributed to controlled drug release and the patches have shown promise in providing sustained drug release profiles [20, 21]. Metoprolol succinate serves as a model drug in this research, known for its solubility, cardiovascular applications, and sustained release formulations [22].

In our previous work we have found that maghemite nanoparticles acts as a compatibilizer the 10/90 GG/MC blend composition [23]. This research work is aimed at studying the transdermal sustained drug release kinetics from the GG/MC blend – γ-Fe_2O_3 nanocomposite thin films using metoprolol succinate as the sample drug.

2. EXPERIMENTAL PROCEDURE:

In this study, Metoprolol succinate drug solutions were prepared, incorporating guar gum (GG), methyl cellulose (MC), their respective γ-Fe_2O_3 nanocomposites, and a 10/90 GG/MC blend - γ-Fe_2O_3 nanocomposite. Each solution, 50 mL in volume, was dispensed into uniformly sized polypropylene petri dishes. Subsequently, thin films were created within a dust-free environment, with each 1 cm^2 patch containing approximately 39.339 µg of the drug. After drying, the films were carefully peeled from the substrate and subjected to analysis.

The thickness, weight, and other physicochemical parameters were measured with three identical samples and the average is taken. The percentage moisture absorption and moisture loss were calculated as per the procedure and using an appropriate formula [24].

The drug release studies were done using Systronics-2202 model spectrometer and open diffusion tube method. The Higuchi [25] and Korsmeyer-Peppas models [26] were applied to the release kinetics data to analyze the underlying drug release mechanisms, with n values indicating Fickian or anomalous diffusion, and $n \geq 1$ signifying zero-order release [26, 27].

3. RESULTS AND DISCUSSIONS:

3.1. Physicochemical evaluations

Table 1 presents the physicochemical evaluation data for metoprolol-infused GG, MC, their γ-Fe_2O_3 nanocomposites, and 10/90 GG/MC blend - γ-Fe_2O_3 films. The thickness ranged from 0.087 to 0.092 mm, with a nearly consistent weight of 218 to 223 mg. Folding endurance spanned 308 to 360, indicating robust strength. Methylcellulose exhibited higher folding endurance than natural guar gum, while maghemite nanoparticles slightly reduced it. These values affirm the usability of these patches for TDRS applications.

Table 1: Physicochemical parameters

Composition	Thickness (mm)	Weight (mg)	FE	PMA	PML

GG	0.089 ± 0.0024	221.000 ± 1.549	314 ± 2	7.72 ± 0.80	3.16 ± 0.03
MC	0.087 ± 0.0012	218.167 ± 1.169	360 ± 2	4.56 ± 0.44	1.38 ± 0.00
GG – γ-Fe_2O_3 composite	0.092 ± 0.0021	223.000 ± 1.095	308 ± 2	6.60 ± 0.28	2.38 ± 0.25
MC – γ-Fe_2O_3 composite	0.091 ± 0.0018	222.167 ± 0.753	316 ± 2	4.51 ± 0.46	1.50 ± 0.26
10/90 GG/MC blend – γ-Fe_2O_3 composite	0.087 ± 0.0018	218.000 ± 0.632	315 ± 1	5.19 ± 0.25	2.14 ± 0.27

To evaluate the structural durability of the thin films under both humid and dry conditions, standard protocols were followed to determine the percentage of moisture absorption and moisture loss. Remarkably, the inclusion of maghemite nanoparticles demonstrated an enhancement in both moisture absorption and moisture loss capacities within the thin films. Specifically, the analyzed samples displayed a moisture absorption percentage spanning from 4.51 to 7.72, accompanied by a moisture loss percentage ranging from 1.50 to 3.16.

3.2. TDRS kinetics

Figure 1 illustrates the drug release profiles from the thin films composed of GG, MC, their corresponding maghemite nanocomposites, and the 10/90 GG/MC blend - maghemite nanocomposites. Through the diffusion analysis, it was evident that the release of the drug from methylcellulose occurred rapidly as compared to guar gum. Notably, the maghemite nanocomposites formed with both methylcellulose and guar gum exhibited a sustained release pattern, contrasting with the immediate release of their pristine polymers. Furthermore, the drug release profile of metoprolol succinate from the 10/90 GG/MC blend - maghemite nanocomposite also demonstrated sustained behavior.

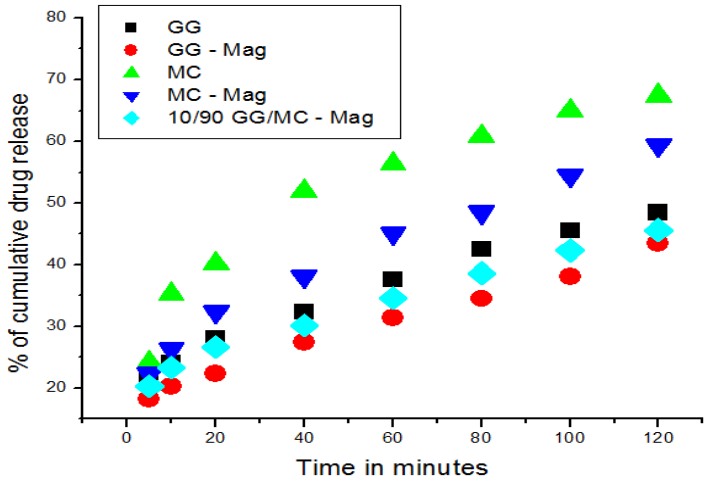

Fig. 1: Drug release kinetic data

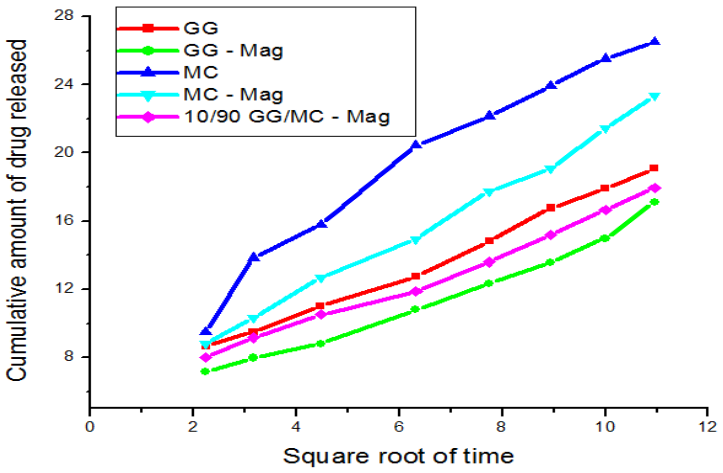

Fig. 2: Higuchi kinetics plot

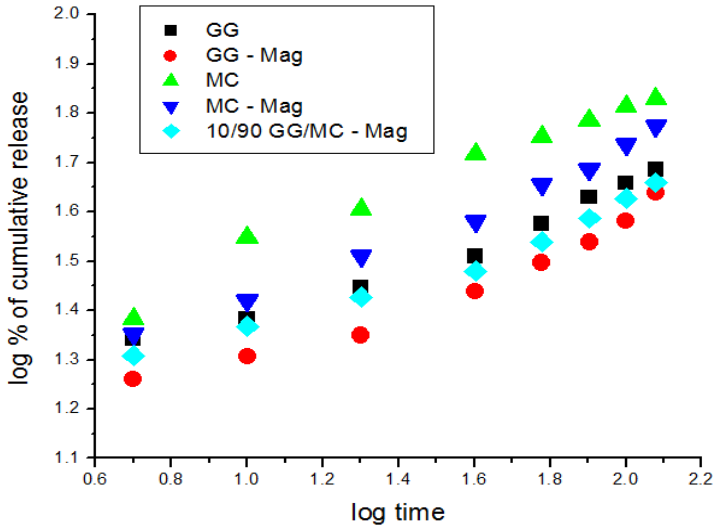

Fig. 3: Koresmeyer-Peppas kinetics plot

Table 2: The values from Koresmeyer-Peppas plot

Composition	Koresmeyer-Peppas model	
	Intercept (k)	Diffusion exponent (n)
GG	1.13636	0.25421
GG – γ-Fe_2O_3 composite	1.04097	0.2655
MC	1.20336	0.30718
MC – γ-Fe_2O_3 composite	1.12308	0.30138

10/90 GG/MC blend – γ-Fe_2O_3 composite	1.1159	0.248

The examination of drug release against the square root of time, utilizing the Higuchi method, serves to discern the release nature. A linear plot indicates diffusion control of the system [26]. Notably, the cumulative drug release versus square root of time plot (depicted in Figure 2) demonstrated linearity across all systems, affirming diffusion as the dominant release mechanism.

Subsequently, the experimental data obtained from in vitro release studies were fitted to the Korsmeyer-Peppas model. The resulting plot (illustrated in Figure 3) facilitated the determination of diffusion exponent "n" and constant "k," as outlined in Table 2. In all instances, the value of intercept "k" exceeded 0.5, while "n" was less than 0.5. These findings collectively support the conclusion that the drug release adhered to Fickian kinetics [26, 27]. As a result, these biomaterials hold potential for the formulation of controlled-release transdermal systems, offering slow and sustained drug release capabilities.

4. CONCLUSION:

This research investigated the potential of biocompatible polymers, guar gum and methyl cellulose, along with maghemite nanocomposites, for transdermal sustained drug release applications. Physicochemical evaluations showcased the suitability of these materials for patch formulation, with thickness, weight, and folding endurance values within desired ranges. The incorporation of maghemite nanoparticles showed improvements in moisture absorption and loss properties of the thin films. The transdermal drug release kinetics demonstrated distinct profiles, with methyl cellulose releasing the drug rapidly, while guar gum and maghemite nanocomposites exhibited sustained release behavior. The data fitting using Higuchi's and Koresmeyer-Peppas models confirmed diffusion-controlled release, indicative of Fickian kinetics. These findings underscore the potential of these biomaterials for developing effective and controlled transdermal drug delivery systems.

ACKNOWLEDGEMENT:

The corresponding author Prasad P. acknowledges the financial support by Vision Group on Science and Technology (VGST, CISEE – GRD No. 538), Government of Karnataka, India.

REFERENCES:

[1] Veeran Gowda Kadajji, Guru V. Betageri. (2011). Water Soluble Polymers for Pharmaceutical Applications, Polymers, 3(4), 1972-2009.

[2] Prasad, P., Guru, G. S., Shivakumar, H. R., & Rai, K. S. (2012). Investigation on Miscibility of Sodium Alginate/Pullulan Blends. *Journal of Polymers and the Environment*. *20*(3), 887-893.

[3] Prasad, P., Guru, G. S., Shivakumar, H. R., & Rai, K. S. (2008). Miscibility, Thermal, and Mechanical Studies of Hydroxypropyl Methylcellulose/Pullulan Blends. *Journal of Applied Polymer Science*. *110*(1), 444-452.

[4] Guru, G. S., Prasad, P., Shivakumar, H. R., & Rai, S. K. (2008). Studies on the Compatibility of Pullulan – Carboxymethyl Cellulose Blend Using Simple Techniques. *Malaysian Polymer Journal*. *3*(2), 13-23.

[5] Guru, G. S., Prasad, P., Shivakumar, H. R., & Rai, S. K. (2010). Miscibility and thermal studies of PVP/Pullulan blends. *International Journal of Plastics Technology*. *14*(2), 234-245.

[6] Guru, G. S., Prasad, P., Shivakumar, H. R., & Rai, S. K. (2010). Miscibility Studies of Polysaccharide Xanthan Gum/PVP Blend. *Journal of Polymers and the Environment*. *18*(2), 135-140.

[7] Bhat, V., Shivakumar, H. R., Sheshappa Rai, K., Ganesh, S., Prasad, P., & Guru, G. S. (2011). Miscibility and Thermal Behavior of Pullulan/Polyacrylamide Blends. *Journal of Macromolecular Science, Part A*. *48*(11), 920-926.

[8] J. Urquhart. (2001). Controlled drug delivery: therapeutic and pharmacological aspects, Journal of Internal Medicine, 249 (S741), 75-94.

[9] Vishwanath Bhat, Shivakumar, H. R., Sheshappa Rai, K., Sanjeev Ganesh, Prasad, P., Guru, G. S., & Bhavya, B. B. (2012). In-vitro release study of metoprolol succinate from the bioadhesive films of pullulan-polyacrylamide blends. *International Journal of Polymeric Materials*. *61*(4), 300-307.

[10] Yogeshvar N. Kalia, Richard H. Guy. (2001). Modeling transdermal drug release, Advanced Drug Delivery Reviews, 48 (2–3), 159-172.

[11] M. Prabaharan. (2011). Prospective of guar gum and its derivatives as controlled drug delivery systems, International Journal of Biological Macromolecules, 49 (2), 117-124.

[12] Bhavya, M. S., Savitha, M. B., & Prasad, P. (2017). Miscibility studies of GG/CMC blends in aqueous solution. *International Journal of Advance Research in Science and Engineering*. *6*(1), 514-523.

[13] Prasad, P., Bhavya, M. S., Abhijith, P. P., Sreelakshmi, S. K., & Savitha, M. B. (2017). Miscibility studies of GG/PVA blends in aqueous solution. *International Journal of Advance Research in Science and Engineering*. *6*(9), 1-8.

[14] Bhavya, M. S., Sudhanva Narayana, K. S., Savitha, M. B., & Prasad, P. (2020). Biocompatible Maghemite Nanoparticles Compatibilization of GG/CMC Blends in Aqueous Solution. *International Journal of Applied Engineering and Management*. *4*(1), 184-190.

[15] Bhavya, B. B., Shivakumar, H. R., Vishwanath Bhat, Prasad, P., & Guru, G. S. (2013). Investigation of miscibility of biocompatible guar gum/pullulan polymer blend. *Malaysian Polymer Journal*. *8*(1), 33-37.

[16] Mitali Dewan, Biplab Bhowmick, Gunjan Sarkar, Dipak Rana, Mrinal Kanti Bain, Manas Bhowmik, Dipankar Chattopadhyay. (2015). Effect of methyl cellulose on gelation behavior and drug release from poloxamer based ophthalmic formulations, International Journal of Biological Macromolecules, 72, 706-710.

[17] Guru, G. S., Prasad, P., Shivakumar, H. R., & Rai, S. K. (2012). Miscibility, Thermal, and Mechanical Studies of Methylcellulose/Poly(vinyl alcohol) Blends. *International Journal of Research in Pharmaceutical Chemistry*. *2*(4), 957-968.

[18] Katarzyna Rudzka, Ángel V. Delgado, Julián L. Viota. (2012). Maghemite Functionalization for Antitumor Drug Vehiculization, Molecular Pharmaceutics, 9 (7), 2017-2028.

[19] Bhavya, M. S., Sudhanva Narayana, K. S., Prasad, P., Savitha, M. B. (2020). Miscibility Studies of Biocompatible Xanthan Gum/Methylcellulose Blend-Maghemite Nanocomposite, *Palarch's Journal of Archaeology of Egypt/Egyptology*. *17*(9), 7720-7735.

[20] Prasad, P., Bhavya, M. S., Abhijith, P. P., Sreelakshmi, S. K., & Savitha, M. B. (2017). Physico-chemical and thermal property studies of GG/CMC blend thin films. *International Journal of Advance Research in Science and Engineering*. *6*(6), 572-578.

[21] Prasad, P., Bhavya, M. S., Nagesh Bhat, Momin Ashraf, Krishnaraja Acharya, & Savitha, M. B. (2018). Physico-chemical and thermal property studies of GG/PVA blend thin films. *International Journal of Advance Research in Science and Engineering*. *7*(1), 1-7.

[22] Khobragade, D. S., Vighneshwar, K., Potbhare, M. S. (2022). Development and Evaluation of Novel Multi-unit Pellet System Formulation of Metoprolol Succinate for Extended Release, International Journal of Drug Delivery Technology, 12 (3), 1219-1227.

[23] Bhavya, M. S., Sudhanva Narayana, K. S., Savitha, M. B., & Prasad, P. (2020). Guar gum (GG)/methylcellulose (MC) blends and their composites with maghemite nanoparticles. *International Journal of Management and Humanities*. *4*(9), 96-102.

[24] Sarath Chandiran I., Jayaveera, K. N., & Saravanan, G. (2014). Formulation and evaluation of controlled release matrix Transdermal patches of Metoprolol Succinate. International Journal of Research in Pharmaceutical Sciences, 5 (1), 85-93.

[25] Higuchi, T. J. (1963). Mechanism of sustained- action medication. Theoretical analysis of rate of release of solid drugs dispersed in solid matrices, Journal of Pharmaceutical Sciences, 52 (12), 1145-1149.

[26] Koresmeyer, R. W., Gurney, R., & Peppas, N. A. (1983). Mechanisms of solute release from porous hydrophilic polymers, International Journal of Pharmaceutics, 15 (1), 25-35.

[27] Kamlesh Kumari, Charu Sharma, & Patit Kundu, P. (2009). In-vitro Release of Metformin Hydrochloride from Films of Chitosan- methylcellulose Blends, Asian J. Chem., 21 (10), 148-152.