Since 1987
REVIEW OF CLINICAL PHARMACOLOGY AND PHARMACOKINETICS, INTERNATIONAL EDITION | 38 (Sup2):35-38 (2024) Rcpp

Received: 5 February 2024 | **Accepted**: 12 February 2024 | **Published**: 5 May 2024

Open Access | Research

Preparation and characterization of nanoparticles loaded with dimethyl fumarate for the treatment of multiple sclerosis

Abdulazeez Basim A. Alhussein[1], Tayser Sumer Gaaz[2,*], Ahed Hameed Jaaz[3]

[1]Faculty of Engineering and Built Environment, Universiti Kebangsaan Malaysia, Bangi, Malaysia
[2]Prosthetics and Orthotics Engineering Department, College of Engineering and Technologies, Al-Mustaqbal University, Babylon, Iraq
[3]Medical Physics Department, College of Science, Al-Mustaqbal University, Babylon, Iraq

***Corresponding author:** Tayser Sumer Gaaz, Prosthetics and Orthotics Engineering Department, College of Engineering and Technologies, Al-Mustaqbal University, Babylon, Iraq; Tel.: +964-(0)7737648546
E-mail: tayser.sumer.gaaz@uomus.edu.iq

Abstract

When nanotechnology is used in medicine, it makes it easier to find and treat a wide range of diseases. One of the oral options for treating multiple sclerosis (MS) is dimethyl fumarate (DMF). DMF has been shown to be effective in lowering inflammatory diseases; nevertheless, it is characterized by several undesirable side effects that reduce patient compliance and add financial obstacles. The aim of this study was to use platelet membranes and platelet nanoparticles to generate a drug delivery system that works like a cell, so as to treat MS. During the experiments, there is a chance that the DMF solution might harden at room temperature. Therefore, in order to produce solid lipid nanoparticles (SLNs), DMF was combined with biocompatible lipids. The creation of SLNs involved the use of hot emulsion and ultrasonication. These DMF-SLNs were characterized by means of scanning electron microscopy, and Fourier-transform infrared spectroscopy. The herein demonstrated enhanced qualities of the devised SLNs suggest that the formulation may be a potential, longer-acting formulation for the improved management of MS. SLNs could change the way many illnesses are treated in a big way, if they are used for the delivery of medicines.

KEYWORDS

multiple sclerosis, dimethyl fumarate, immunomodulatory fumaric acid, solid lipid nanoparticles, microphotograph

How to cite: A. Alhussein A. B., Gaaz T. S., Jaaz A. H. Preparation and characterization of nanoparticles loaded with dimethyl fumarate for the treatment of multiple sclerosis. *Rev. Clin. Pharmacol. Pharmacokinet. Int. Ed.* 38 (Sup2): 35-38 (2024).
https://doi.org/10.61873/CNAY1739

Publisher note: PHARMAKON-Press stays neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Copyright: © 2024 by the authors.

Licensee PHARMAKON-Press, Athens, Greece.
This is an open access article published under the terms and conditions of the Creative Commons Attribution (CC BY) license.

1. INTRODUCTION

Multiple sclerosis (MS) is an advanced illness of the central nervous system that is characterized by the collapse of the myelin sheath [1]. Dimethyl fumarate (DMF), also known as fumaric acid, exhibits antioxidant and immunomodulatory properties, and is used as an oral treatment for recurrent MS. In fact, DMF is a medication licensed for treating MS and psoriasis due to its antioxidative and anti-inflammatory properties. Moreover, its posi-

tive benefits have also been identified in other inflammatory disorders as well as in malignancies. Unfortunately, several disease-modifying treatments, including DMF for treating MS, have been linked to the development of progressive multifocal leukoencephalopathy [2].

Biocompatible lipids are used to create solid lipid nanoparticles (SLNs). SLNs are characterized by some desirable properties, such as a large surface area, an elevated drug capacity, and an interface point reaction. The delivery of nanoparticles to specific places is made possible by size-dependent targeting, as the altering of nanoparticles so as to achieve active targeting has been shown to be a successful approach.

2. MATERIALS AND METHODS

Materials: DMF ($C_6H_8O_4$) was purchased from Sigma-Aldrich (Saint Louis, MO, USA). Stearic acid ($C_{18}H_{36}O_7$) was purchased from Merck Schuchardt OHG (Hohenbrunn, Germany). Soya lecithin ($C_{35}H_{66}NO_7P$; palmitic acid 11.7%, stearic acid 4%, palmitoleic acid 8.6%, oleic acid 9.8%, linoleic acid 55%, and linolenic acid 4%) was obtained from Ever Gainful Enterprise Sdn Bhd (Petaling Jaya, Malaysia). Ethanol (C_2H_5OH) was purchased from Chemicals and Pharma Works (Selangor, Malaysia), while Tween 80 (polyoxyethylene sorbitan monooleate; $C_{64}H_{124}O_{26}$) was obtained from Chemsworth Chemicals (Selangor, Malaysia).

Preparation of SLNs: First, 1 g of DMF was sonicated with 30 mL of ethanol. This is the first of five steps. According to Ojha & Kumar [3], the mixture was subsequently boiled at 75°C with 2 g of stearic acid and 250 mg of soy lecithin. The third step involves creating a solution by dissolving 10 mL of Tween 80 in 150 mL of distilled water. In the fourth step, the resultant dispersion is dissolved in cold water at 2–5°C. This is done after 20 min of stirring at 10,000 rpm.

3. RESULTS AND DISCUSSION

Fourier-transform infrared (FTIR) spectroscopy analysis: When FTIR was used on scaffolds with various nanoparticle concentrations, the results did not significantly differ from those obtained with pristine cross-linked DMF resin. Figure 1A displays the FTIR spectra of our DMF nanoparticles. The coordination of unsaturated surface DMF atoms with hydroxyl ions or water molecules in the aqueous media results in the formation of OH groups, which alter the surface chemistry of magnetite nanoparticles. The aromatic C-H bending vibration that causes the peak for DMF at 990.22 cm^{-1} was seen in both films, but the adjacent H deformation at 1,159.64 cm^{-1} and the aromatic C=O stretching at 1,308 and at 1,438.90 cm^{-1}, as well as the C=O stretching for ester anhydride at 1,715.97 cm^{-1} and the O-H stretching at 3,428.77 cm^{-1} in the film samples did not match with what was seen in the pure drug sample, while the aromatic C-H stretching was noted at 3,076.50 cm^{-1}, as shown in Figure 1A. SLNs-1 displayed an aromatic C-H bending at 944.42 cm^{-1}, H deformation at 1,472.19 cm^{-1}, aromatic C=O stretching at 1,703.96 and at 2848.93 cm^{-1}, C=O stretching for ester anhydride at 2,916.94 cm^{-1}, O-H stretching at 3,649.46 cm^{-1}, and aromatic C-H stretching at 3,858.50 cm^{-1}, as shown in Figure 1B (teal colour). SLNs-2 displayed an aromatic C-H bending at 943.04 cm^{-1}, H deformation at 1,471.89 cm^{-1}, aromatic C=O stretching at 1,701.40 and at 2,848.38 cm^{-1}, C=O stretching for ester anhydride at 2,916.02 cm^{-1}, and O-H stretching at 3,505.05 cm^{-1}, as shown in Figure 1B (pink colour). Finally, SLNs-3 displayed the following characteristics: aromatic C-H bending at 944.11 cm^{-1}, H deformation at 1,472.22 cm^{-1}, aromatic C=O stretching at 1,703.32 and at 2,848.95 cm^{-1}, C=O stretching for ester anhydride at 2,917.15 cm^{-1}, and O-H stretching at 3,436.97 cm^{-1} (Figure 1B; red colour).

In the case of the C-H bend, the current result (944.42 cm^{-1}) is very close to the result presented by Ojha & Kumar [3] (948 cm^{-1}), while it is higher than the result measured by Sinha *et al*. [4] (775.38 cm^{-1}). A possible reason might be due to the shrinking angle between the bonds, as noted by Riaz *et al*. [5]. The current study's H bond (1,472.19 cm^{-1}) is larger than other studies' H bonds: 883.4 [4] and 1,099 cm^{-1} [3], respectively. As explained by Taib *et al*. [6], the change in bond angle between bonds with a typical atom may be a good reason for this result. The C=O bond has shown three values in the current study and the other two studies [3,4]. The sequence of the three stretching vibrations in the current study (1,703.96, 2,848.93, and 2,916.94 cm^{-1}) exhibited higher vibration than that of Sinha *et al*. [4] (1,161.15, 1,199.72, and 1,722.43 cm^{-1}), while it is almost identical to the sequence found by Ojha & Kumar [3] (1,129, 2,850, and 2,918 cm^{-1}). The C=O stretching is the most prominent peak due to the high polarity of single C-O bonds, as previously reported [6]. The values of the O-H bond in the current study (3,649.46 cm^{-1}) are slightly higher than those found by Sinha *et al*. [4] (3,429.43 cm^{-1}). Finally, the last stretching frequency (the C-H stretch) indicated that the C-H stretches can reach values greater than 3,000 cm^{-1}. However, the current study has shown a slightly higher frequency

(3,853.5 cm^{-1}) for this parameter than the value found by Ojha & Kumar [3] (3,400 cm^{-1}).

Field emission scanning electron microscopy (FE-SEM) analysis: The FE-SEM measurements of the surface topography of the SLNs provided a good explanation of their interior structure. The panels a–d of Figure 1C display the FE-SEM pictures of DMF, SLNs-1, SLNs-2, and SLNs-3, respectively. When viewed under a microscope, the prepared DMF films have a surface roughness that resembles nanofibers. These nanofibers included SLNs-1, SLNs-2, and SLNs-3. Nanoparticles were found to have an average size of 500–2,000 nm. Figure 1C reveals that the particles had an unsmooth surface and a spherical shape, and indicates that they were in the nanoscale range.

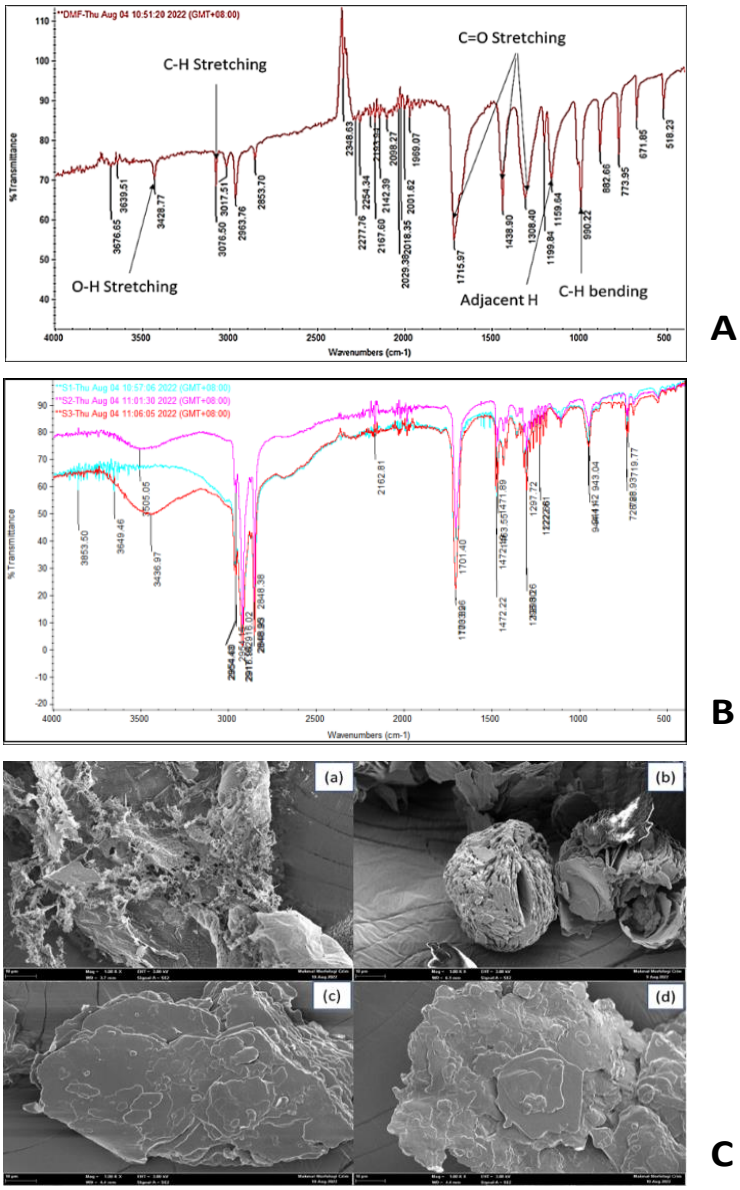

Figure 1. (**A**): Fourier-transform infrared (FTIR) spectrum of dimethyl fumarate (DMF); (**B**): FTIR spectra of three samples of solid lipid nanoparticles (SLNs), namely SLNs-1 (teal colour), SLNs-2 (pink colour), and SLNs-3 (red colour); (**C**): Field emission scanning electron microscopy (FE-SEM) of DMF (a), SLNs-1 (b), SLNs-2 (c), and SLNs-3 (d).

4. CONCLUSION

The present study discusses how to prepare and characterize nanoparticles depending on DMF. The nanoparticles were prepared and assessed for their size and zeta potential. The FTIR spectrum of nanoparticles in varying concentrations was examined. In an attempt to explore the cross-linked nanocomposites, FE-SEM was employed. Our findings suggest that DMF-controlled-loaded-release SLNs may be a good option for treating and managing MS. Meanwhile, the optimized SLNs had a mean particle size of 562, 1,997, and 849 nm. According to the results of this study, the current formulation is a promising, longer-acting formulation for the better management of MS. Moreover, SLNs hold promise as a medication delivery method that can revolutionize the treatment of many diseases.

ACKNOWLEDGEMENTS
This work was supported by the Faculty of Engineering and Built Environment of the Universiti Kebangsaan Malaysia, and by the Al-Mustaqbal University.

CONFLICT OF INTEREST STATEMENT
The authors declare no conflicts of interest.

REFERENCES

1. Ghasemi N., Razavi S., Nikzad E.: Multiple sclerosis: pathogenesis, symptoms, diagnoses and cell-based therapy. *Cell J.* 19(1): 1-10 (2017).
DOI: **10.22074/cellj.2016.4867**
PMID: **28367411**

2. Jordan A.L., Yang J., Fisher C.J., Racke M.K., Mao-Draayer Y.: Progressive multifocal leukoencephalopathy in dimethyl fumarate-treated multiple sclerosis patients. *Mult. Scler.* 28(1): 7-15 (2022).
DOI: **10.1177/1352458520949158**
PMID: **32808554**

3. Ojha S., Kumar B.: Preparation and statistical modeling of solid lipid nanoparticles of dimethyl fumarate for better management of multiple sclerosis. *Adv. Pharm. Bull.* 8(2): 225-233 (2018).
DOI: **10.15171/apb.2018.027**
PMID: **30023324**

4. Sinha S., Garg V., Sonali, Singh R.P., Dutt R.: Chitosan-alginate core-shell-corona shaped nanoparticles of dimethyl fumarate in orodispersible film to improve bioavailability in treatment of multiple sclerosis: preparation, characterization and biodistribution in rats. *J. Drug Deliv. Sci. Technol.* 64: 102645 (2021).
DOI: **10.1016/j.jddst.2021.102645**

5. Riaz S., Al-Abdeli Y.M., Oluwoye I., Altarawneh M.: Torrefaction of densified woody biomass: the effect of pellet size on thermochemical and thermophysical characteristics. *BioEnergy Res.* 15(1): 544-558 (2022).
DOI: **10.1007/s12155-021-10319-8**

6. Taib N.I., Agarwal V., Smith N.M., Woodward R.C., St Pierre T.G., Iyer K.S.: Direct correlation of PNIPAM thermal transition and magnetic resonance relaxation of iron oxide nanoparticles. *Mater. Chem. Front.* 1: 2335-2340 (2017).
DOI: **10.1039/C7QM00202E**