MODELING THE ENCAPSULATION OF TURMERIC IN NANOEMULSIONS

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The interaction of turmeric powder with five surfactants (isopropyl oleate, diester of sucrose, polymethylene-α, ω-bis (N, N-dialkyl-N-deoxy-d-glucitolammonium iodides, bis [2-butyl (sodium bis-thioacetate) sodium dicarboxylate 1,10 decanediyl] ester, demecarium bromide) and obtaining nanoemulsions, has been investigated by spectroscopy, dynamic light scattering, optical microscopy and microbiological tests. The modeling encapsulation of turmeric powder in nanoemulsions was carried out taking into account the following parameters: the concentration and type of surfactants, the ratio between turmeric and surfactant, micellar critical concentration, speed and time of stirring, temperature, pH, average diameter of particles, zeta potential, conductivity. The known antibacterial and anti-inflammatory properties of turmeric can be improved by dispersing it in nanoemulsions resulting in better functional efficacy. The specific factors in designing nanoemulsion systems that affect the chemical stability of the encapsulated turmeric are discussed. In order to enhance turmeric effectiveness and improve bioavailability, surfactant assemblies as the colloidal carriers with desired properties have been largely used. The interaction takes place above the critical concentrations of the surfactants, when the encapsulation/ solubilization of turmeric in the micelles occurs. In our research we have elaborated a method for including turmeric in surfactants, following the preparation parameters modeling with the final aim of developing enhanced antibacterial properties.

Keywords: encapsulation, nanoemulsions, modelling the interaction of turmeric with surfactants

INTRODUCTION

Turmeric gets its health benefits primarily because of curcumin, a bioactive component. Curcumin (1,7-bis(4-hydroxy-3-methoxyphenyl)-1,6-heptadien-3,5-dione called as diferuloylmethane) is a bioactive constituent of turmeric, the Indian spice, obtained from the "*Curcuma longa*" rhizome and has been known for centuries as a household remedy to many ailments. Modern scientific research works (Das *et al*., 2022; Hughes *et al*., 2021; Nuraje *et al*., 2013; Varasteanu, 2014; Bungay and Smolders, 1986) are just beginning to study the positive impact of turmeric for leather. Clinical development of turmeric is mainly hindered due to its low aqueous solubility (20 μg/mL) which can be improved by increasing the pH of the solution. Surfactant micelles are largely used as colloidal carriers by encapsulation of the drugs (like turmeric) in order to ensure the transport to specific sites of action, to minimize drug degradation and loss. Therefore, the study of drug (like turmeric)–surfactant interactions has received an increased attention lately. In this research the interactions of 5 surfactants (gemini, bola and classical) with turmeric compared to a control sample (turmeric in water) at pH=6, was studied by: UV/VIS spectroscopic technique, dynamic light scattering, optical microscopy, microbiological tests and proposed the mechanisms of turmeric-surfactants interactions at low, intermediate, and high surfactant concentration region, which is relating to interaction forces, surfactant aggregations, as well as structural alterations of turmeric. DLS investigations showed a favourable thermodynamic stability of turmeric in the five micellar systems used. The surfactant-turmeric molecular interaction was determined on the basis of shift in absorption UV/VIS spectra of the turmeric when going from an aqueous to a more hydrophobic environment at various concentrations of surfactant. The mechanism of surfactant-turmeric interaction has been proposed at pre-micelles, intermediate, and post-micellar surfactant concentrations regime, which relate to various attractive and repulsive forces

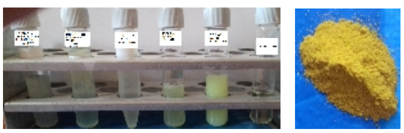
https://doi.org/10.24264/icams-2022.I.9

arising, structure and aggregations of surfactant, as well as structural alterations of turmeric. The mechanism proposed for surfactant-turmeric interaction may be used as model for several systems when gemini or bola tensides and turmeric were utilized.

EXPERIMENTAL

Materials and Methods

In order to obtain nanoemulsions with turmeric encapsulated (Fig. 1), the following materials have been used: turmeric powder (*Curcuma longa*) from Sigma-Aldrich; isopropyl oleate – classical surfactant from Sigma-Aldrich; diester of sucrose-gemini 1 from SERVA Feinbiochemica GmbH & Co; sugar-based gemini surfactant (polymethylene-α,ω-bis(N,N-dialkyl-N-deoxy-d-glucitolammonium iodides) – gemini 2 from SERVA Feinbiochemica GmbH & Co; bis [2-butyl (sodium bis-thioacetate) sodium dicarboxylate 1,10 decanediyl] ester-BOLA 1, obtained in an original method at ICECHIM in an PhD Thesis (Varasteanu, 2014); demecarium bromide – bola 2 from Sigma-Aldrich; ethanol is of AnalaR grade. Phosphate buffer solution (PBS) of pH 6 is prepared in the laboratory by dissolving of potassium dihydrogen phosphate in water adjusting the pH with 1.0 M potassium hydroxide and diluting to 1.0 L with water. Triple distilled deionized water for sample preparation and all-PyrexTM glass apparatus was always used. The experimental techniques used consist in: UV/VIS spectrophotometer (V-550, JASCO) for UV/VIS spectroscopy; BS-2082 Research Biological Microscope, Magnification:40x-1000x for optical microscopy; "MALVERN" zetasizer-nano equipment, with measuring range between 0.3 nm – 60.0 microns and zeta potential determination with an accuracy of +/-2%. A number of 5 samples of: turmeric powder/surfactant (gemini, bola and classical)/ ethanol/water compared with a control sample (turmeric in water) – sample 6, were prepared in the working conditions: water-ethanol solvents at 1:1 ratio, temperature=75°C for 60 minutes with turmeric powder-c=0.1%; surfactant concentration-c=0.3%, at pH=6 adjusting with a phosphate buffer solution (PBS), speed at 200 rot/min, HLB from 7 to 10, Fig. 1. The samples in this research are: sample 1 – turmeric powder/ isopropyl oleate-classical tenside/ethanol/water; sample 2 – turmeric powder/sucrose diester- Gemini 1/ethanol/water; sample 3 – turmeric powder/ polymethylene-α,ω-bis(N,N-dialkyl-N-deoxy-d-glucitolammonium iodides-Gemini 2/ ethanol/water; sample 4 – turmeric powder/ bis [2-butyl (sodium bis-thioacetate) sodium dicarboxylate 1,10 decanediyl] ester-Bola 1/ ethanol/water; sample 5 – turmeric powder/ demecarium bromide – Bola 2/ethanol/water; sample 6 – control sample with turmeric powder/water.



a) 1 2 3 4 5 6 b)

Figure 1. a) Photographic image of 6 samples; b) Image of turmeric powder

RESULTS AND DISCUSSIONS

Obtaining Emulsions with Turmeric Encapsulated

The encapsulated of turmeric in emulsions is a two-step emulsification process. The result are multiple emulsions with turmeric encapsulated due to the properties of the

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five surfactants (gemini, bola and classical) used, to orient and form emulsions at the nano and micro levels. Multiple emulsions are complex systems, also called ‘emulsions of emulsions’, in which the dispersed phase droplets contain a continuous phase with other dispersed droplets. The main types of multiple emulsions are water-oil-water and oil-water-oil. In the first step (I) introduction in water/ethanol at 1:1 ratio, the surfactant (c=0.3%) with HLB from 7 to 10, by homogenized and stirring at 75°C for 60 minutes, speed at 200 rpm, to obtain a water-oil emulsion. In second step (II) turmeric powder is added at c=0.1%, pH=6 adjusting with a phosphate buffer solution (PBS), to create water-oil emulsion, and homogenized by stirring at 75°C, for 60 minutes, speed at 200 rpm obtaining a multiple water-oil-water emulsion (W/O/W) with turmeric encapsulated. Multiple emulsions are fragile systems, so the choice of emulsification methods is of particular importance in the success of obtaining the dispersed-turmeric in emulsions with the desired properties.

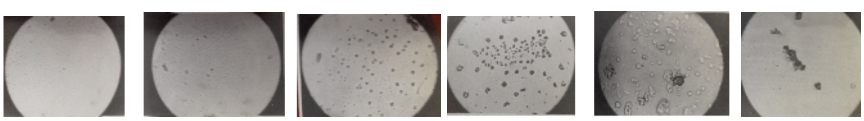
Characteristics of Emulsions with Turmeric Encapsulated

Dynamic Light Scattering (DLS)

A number of five samples of: turmeric powder/surfactant (gemini, bola and classical)/ ethanol/water compared with a control sample (turmeric in water) – sample 6, were characterized by dynamic light scattering. Dynamic light scattering tests showed that all five emulsions with turmeric are nano and microstructured. The size, percentage of the particles and Zeta potential were determined (indicating their stability). From the five selected surfactants, it was found that the best dispersion of turmeric in emulsions created was achieved in the following descending order for: polymethylene-α,ω-bis(N,N-dialkyl-N-deoxy-d-glucitolammonium iodides – Gemini 2 (particle diameter=0.72 nm)>isopropyl oleate-classical tenside (particle diameter=52.4 nm)>diester of sucrose – Gemini 1 (particle diameter=81.3 nm)> demecarium bromide – Bola 2 (particle diameter=98.2 nm) > bis [2-butyl (sodium bis-thioacetate) sodium dicarboxylate 1,10 decanediyl] ester – Bola 1 (particle diameter=98.6 nm). Zeta potential without dilution and stirring for 5 minutes showing a tendency to agglomerate. The influence of surfactants facilitates obtaining stable emulsions with turmeric encapsulated.

Optical Microscopy Tests

The optical microscopy images from Fig. 2, showed the five emulsions with turmeric encapsulated, samples compared with control sample 6. All five emulsions presented in Fig. 2 had a good turmeric encapsulation process. Fig. 2 shows oriented and agglomerated structures. The results are in agreement with literature data (Das *et al*., 2022; Hughes *et al*., 2021; Nuraje *et al*., 2013; Varasteanu, 2014) related to the formation of structures in multiple water-oil-water emulsions.



Sample 3 Sample 1 Sample 2 Sample 5 Sample 4 Sample 6

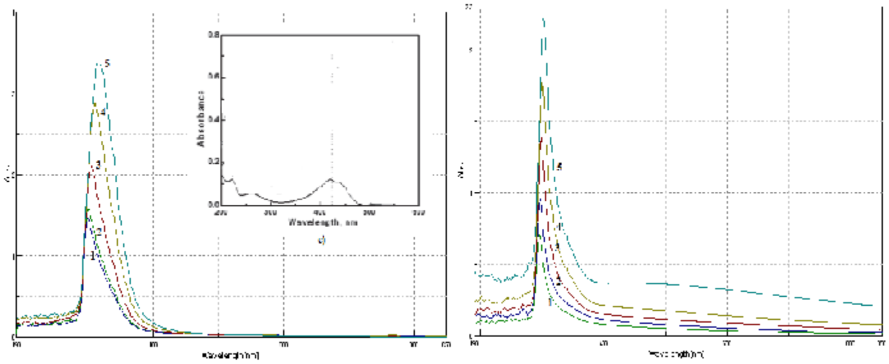
Figure 2. Optical microscopy images (1000x) for samples 1-6

The best dispersion for turmeric was in sample 3 with polymethylene-α, ω-bis (N, N-dialkyl-N-deoxy-d-glucitolammonium iodides-Gemini 2. Fig. 2 shows, in descending order, turmeric dispersion samples and sample 6 (control) is turmeric agglomerated in solvents.

https://doi.org/10.24264/icams-2022.I.9

UV-VIS Spectroscopy Tests

An UV/VIS spectrophotometer (V-550, JASCO) was used for tests. All the analyzed emulsions: 1-5 (Fig. 3) have a rightward displacement of the absorption maxima due to the presence of surfactants (bola, classical and gemini).



a) *b)*

Figure 3. Overlapping UV-VIS spectra in pre-micellar regions a) and post-micellar b) of samples: 1-5; c) UV/VIS fingerprint spectra of turmeric in ethanol/water at 420 nm

Absorption spectra of turmeric (at fixed 10μm concentration) were in the range of 200 to 600 nm. Blank turmeric calibration curves were developed by dissolving a given amount of turmeric in ethanol followed by the required dilution by water. The presence of ethanol did not alter either the extinction co-efficient or the specific wavelength at which the maximum in UV absorbance appeared. The UV-VIS absorbance fingerprint spectra of turmeric (without surfactant), in water/ethanol are shown in Figure 3-c. Turmeric has the absorption peak at 420 nm, which indicates an increase in intensities with turmeric concentrations. Calibration with dilute solutions of the turmeric in water/ethanol gave satisfactory Beer–Lambert plot with R^2 = 0.98161.

Microbiological Tests

The 6 samples were also microbiologically analysed, to determine behaviour to bacterial attack of *Staphylococcus aureus* and *Escherichia coli*, carrying out analysis three days from inoculations. The best results were obtained both for *Staphylococcus aureus* and *Escherichia coli* for samples 3>1>2.

The Mechanism Proposed for Interaction of Surfactant with Turmeric

The interaction of turmeric with five surfactants (gemini, bola and classical) was investigated using UV-VIS absorption spectroscopy, DLS and optical microscopy. The results have outlined three distinct processes depending on the surfactant concentration. In the pre-micellar range, the variation of the absorbance and peak was assigned to attraction of initially positive head group towards the b-diketone group of turmeric. At surfactant concentration in intermediate/micellar region including CMC, a second type of interaction is observed, corresponding to the attachment of alkyl chains of surfactant to aryl groups of turmeric and displacement of head group from b-diketone group of the turmeric. Finally at surfactant concentration higher than the CMC, in the postmicellar region, a type of interaction is observed, which corresponds to the encapsulation/ solubilization of the turmeric into micelles, predominantly in monomeric form (Fig. 4).

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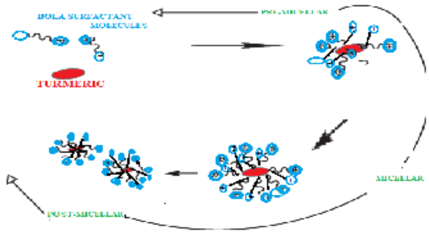

Figure 4. Schematic presentation of a mechanism proposed, of interaction between turmeric and Bola surfactant molecules (with positive charge)

Modeling the Encapsulation Process of Turmeric in Emulsions

Modeling encapsulation of turmeric in emulsions was carried out taking into account all the parameters: the concentration and type of surfactants, the ratio between turmeric and surfactant, micellar critical concentration, speed and time of stirring, temperature, pH, average diameter of particles, zeta potential, conductivity (Fig. 5).

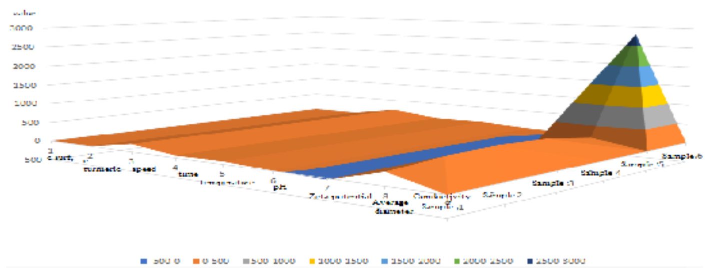

Figure 5. Schematic representation of modelling process, proposed, with all parameters for the six samples obtained

In this research the speed yield of turmeric in water (which is encapsulated in emulsions) was modeled for the best results of samples: 3 and 1. The dependence of absorbance to the encapsulated turmeric from samples 3 and 1, yielded in water, on the time (at λ= 420 nm), was also analysed. The calculation modeling program created is in VBA with the Excel Worksheet interface. For sample 1, the speed yield in water of turmeric encapsulated in emulsions, according to the modeling program is: v= 0.0000023214 units of Abs/min (0.23214 $.10^{-5}$ units of Abs/min). For sample 3, the speed yield in water of turmeric encapsulated in emulsions, is v= 0.0036596821 units of Abs/min. Program modeling indicates that speed yield of turmeric in water encapsulated in emulsions is different depending on the type of surfactant used and its interaction with turmeric. The modeling of release speed in water, of turmeric encapsulated in emulsions, can be done based on (Bungay and Smolders, 1986). In Table 1 the theoretical results of three models on a data set (for sample 3) are presented comparatively, and in Figure 6, the comparative graphic representation.

Table 1. Comparison of failure profiles (Bungay and Smolders, 1986)

	$S.10^5$	a	σa	b	σb	c	σc
Zero order	4.4	0.496645	5.39E-05	-0.00015	1.97E-05		
Order one	2.41	0.49589	0.000156	0.000956	8.46E-05	0.407194	0.173009
Radical order	2.32	0.496968	4.93E-05	-0.00045	3.12E-05		

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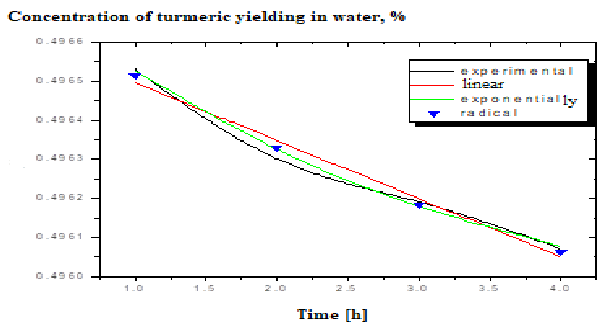

Figure 6. Comparison of yield profiles

The first order failure profile was chosen because there are 2 values of the absorbance (initial and final), and the failure of speeds yield of turmeric in water is very low. The modeling of release speed in water of turmeric encapsulated in emulsions can be done based on the first-order profile.

CONCLUSIONS

Turmeric powder has low aqueous solubility and the solution of this research is to encapsulate it in nanoemulsions with surfactants. Turmeric encapsulated in nanoemulsions applied to leather may revive it by bringing out its natural glow, luster and enhance its antibacterial properties due to the antioxidans and antiinflammatory components. The mechanism of interaction for surfactant-turmeric was created. Also, the encapsulation of turmeric powder in nanoemulsions was modeled taking into account all the parameters.

Acknowledgements

The present work was supported by the Romanian Ministry of Research, Innovation and Digitalization, Nucleus Program, project PN 19 17 01 02/ 2022, contract 4N/2019; project E!12610, project number PN-III-P3-3.5-EUK-2017-D-0098, FERTI-MAIZE, contract 127/2020, within PNCDI III; project number PN-III-P3-3.5-EUK-2019-0237 within PNCDI III (NonActivPans), Contract 219/23.12.2020; and project 4 PFE/2022.

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