Journal of Microencapsulation, 2011; 28(3): 159–165

ISSN 0265-2048 print/ISSN 1464-5246 online
DOI: 10.3109/02652048.2010.520092

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Photostabilization of sunscreen oil through preparation of a free-flowing powder

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Abstract

Octyl-p-methoxycinnamate (OMC) is a sun-blocking agent that absorbs ultraviolet (UV) radiation in UVB range. However, when exposed to sunlight, OMC is converted into a less UV-absorbent form, which reduces its effectiveness. The aim of this study was to stabilize the oil by microencapsulation and to convert it into a free-flowing powder form. In addition, the study aimed to develop a suitable high-performance liquid chromatography method to detect the oil in the presence of its degradation product. OMC was microencapsulated by the congealable disperse-phase encapsulation using carnauba wax (cw) and beeswax (bw) at different wax-to-drug ratios (2:1 and 4:1). The photostability of the oil was investigated by exposing the microspheres to UV radiation. After 180 min of exposure, the photoprotective abilities of all the tested formulae were similar and reached about 82%. However, physicochemical assessment showed superiority of cw microspheres over their bw analogues.

Keywords: Microspheres, wax encapsulation, octyl-p-methoxycinnamate, sun protection factor, HPLC assay

Introduction

The topical application of sunscreen preparations represents a widespread strategy for protecting the skin against variable types and degrees of damage e.g. erythema, cutaneous photoageing, immune suppression and various forms of skin cancers (Kullavanijaya and Lim, 2005; Gaspar and Maia Campos, 2006). The role of the sunscreen agent is to attenuate the transformation of the solar energy to the skin by absorbing, reflecting or scattering the ultraviolet (UV) radiation (Janjura et al., 2004; Scalia et al., 2006; Gaspar and Maia Campos, 2007).

High photostability represents one of the most important requirements for the efficiency and safety of sunscreen agent (Ramadan et al., 2006). A sunscreen product which loses its capacity to block UV radiation during exposure to the sun provides a clear risk of damage to the user and its use may be more harmful than the protection it affords (Huong et al., 2007). This may be attributed to the fact that the reactive intermediates of photounstable filter substances come into direct contact with the skin, where they may behave as photo-oxidants or may also promote phototoxic or photoallergic contact dermatitis (Gaspar and Maia Campos, 2006).

One of the most widely used sun-blocking agents is octyl-p-methoxycinnamate (OMC). It is approved by the regulatory agencies in Europe. It is classified as an UV-B filter in accordance to its higher absorption in the shorter wavelength region (290–320 nm) of the solar UV radiation (Perguini et al., 2002). However, several studies (Pattanaargson and Limphong, 2001; Pattanaargson et al., 2004; Gaspar and Maia Campos, 2006; Huong et al., 2007) have demonstrated that it is unstable following irradiation both in solution and in emulsion formulations, where it is converted into a less UV absorbent form (Z-octyl methoxycinnamate) as shown in the chemical reaction below.

Many research groups have studied different carrier systems for UV filters. A study done by Alvarez-Román et al. (2001) showed a superior photoprotective ability

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(Received 30 May 2010; accepted 27 Aug 2010)
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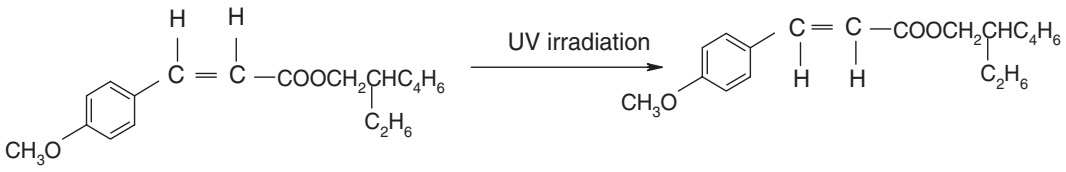

E-octyl methoxy cinnamate Z-octyl methoxy cinnamate

of gel-containing OMC nanocapsules than conventional gels. Wissing and Müller (2002) have also proven an improved photoprotection of crystalline lipid nanoparticles as a carrier for benzophenone-3 over conventional o/w emulsion systems. Other research workers investigated the enhancement of photostability of UV filters through liposphere formulation. Iannuccelli et al. (2006) have found that the incorporation of butyl-methoxydibenzoylmethane in lipospheres decreased the light-induced sunscreen degradation. Tursilli et al. (2006) studied the effect of lipospheres as carrier systems on the light-induced degradation of melatonin. The results showed that the extent of degradation decreased from 19.6% for the unencapsulated melatonin to 5.6% for the melatonin-loaded microparticles. Tursilli et al. (2007) have evaluated the lipospheres of octyl-dimethylaminobenzoate after introducing them in hydrogel and o/w emulsion systems. The hydrogel was found to achieve a reduction in the sunscreen photodegradation, whereas, no significant photoprotective effect was observed for the emulsion.

The aim of this study was to stabilize OMC by microencapsulation and thereby to convert the sunscreen oil into a free-flowing powder form suitable for dry application on the skin. This formulation was claimed to have a double benefit: first, to protect the oil from photodegradation by light; second, to provide an elegant and easy way of application of the oil without the sticky feeling of the conventional lotions.

Furthermore, in order to be able to evaluate the degradation of OMC, a simple isocratic high-performance liquid chromatography (HPLC) method was developed to determine OMC in the presence of its degradation product.

Materials and methods

Materials

OMC was kindly supplied by EVA Cosmetics Lab, Egypt with a given purity of 99.9%. Carnauba wax (cw), beeswax (bw) and Tween 80 were obtained from Adwic, Egypt. The solvents used in the study were methanol (HiPerSov®, HPLC grade, E.Merck, Darmstadt, Germany) and deionized water, bidistilled by Aquatron Automatic Water Still A 4 (Bibby Sterillin Ltd., Staffordshire, UK). All other chemicals were of analytical grade.

Microsphere preparation

Test for syneresis

Each of the tested molten waxes was mixed with the oil at the predetermined ratio and then allowed to solidify together. A spatula was then introduced in the solid matrix and withdrawn to test for bleeding if present and to confirm for the solubility of the oil in the congealed waxes.

Wax encapsulation

Congealable disperse phase was the method adopted to encapsulate the oil (Westesen and Siekmann, 1996). The waxes selected for the study were cw and bw at wax-to-drug ratios 2:1 and 4:1 for each wax. The oil was dissolved in the molten wax. The hot liquid mixture was poured into 100 mL boiling water containing 1% w/w Tween 80. The whole mixture was mechanically homogenized using a high speed homogenizer (MSE Homogenizer, England) equipped with a three-blade system, at 10 000 rpm for 10 min until a white stable emulsion was formed. Ice cooling was then performed on the hot emulsion till congealing and separation of the wax microspheres containing the oil were achieved. The microspheres were collected by filtration, air dried and kept in a desiccator till further investigations.

Physicochemical assessment of the microspheres

Testing for flowability

The flowability of the prepared powder microspheres was tested by measuring angle of repose (Carstensen, 2001; Sinko, 2006), fluff density and bulk density (Sinko, 2006). The data were then used to calculate Carr's compressibility index and Hausner ratio (Wells, 1988; Aulton, 2007).

Measurement of angle of repose. Angle of repose was measured using a glass funnel (diameter: 6.8 cm; stem length: 0.7 cm). The funnel was fixed by a ring stand, such that the bottom of the stem orifice was 2 cm from the bench surface. The outlet of the funnel stem was closed and the funnel was carefully filled with 6 g of the dry microspheres. Then, the contents were allowed to pour out simultaneously. The diameter of the resulted cone was measured and the angle of repose was then calculated (Davis and Gloor, 1971). Microspheres corresponding to each wax-to-oil

ratio were tested and each result was an average of four determinations.

Determination of bulk density. A sample of 50 cm^3 of powder microspheres was poured into a 100 cm^3 graduated cylinder. The cylinder was dropped onto a hard wooden surface nine times from a height of 1 in. The bulk density was then obtained by dividing the weight of the sample in grams by its final volume. The fluff density was also obtained from the weight and the initial volume of the sample.

Evaluation of encapsulation efficiency

An amount of microspheres equivalent to 0.1 g oil for both the tested ratios was weighed, crushed by grinding and suspended in 10 mL methanol. The suspension was stirred for 15 min to ensure complete dissolution of the oil, filtered and assayed for the oil content by HPLC. The evaluation was repeated three times for each formulation.

Scanning electron microscopy

Surface topography, texture and porosity of the microspheres were evaluated by scanning electron microscopy (SEM; Jeol JxA-840A, Japan).

Particle size analysis

A microscope (Leica DMLB, Germany) equipped with a camera (JVC TK-C1380; Japan) and computer-controlled image analysis system (Leica Q550IW, Germany) was used to determine microsphere diameter. The microspheres were dispersed on a microscope slide and the microscopical field was scanned by video camera. The images of the scanned fields were digitalized and analysed for particle diameter by the software Leica QWin (Germany). At least 1000 particles from each formula were examined. The data were used to establish particle size distribution curves.

Determination of sun protection factor

The sun protection factor (SPF) is an indicator that shows protectiveness of sunscreens. Determination of SPF of the formulated microspheres was based upon the *in vitro* spectrophotometric measurement technique described by Diffey and Robson (1989). The principle of this method is to measure the spectral transmission of UV radiation through a sunscreen preparation applied on a transpore tape. The transpore tape provides an irregular surface that distributes the topically applied sunscreen in much the same way as human skin (Diffey and Robson, 1989).

A piece (4.5 cm^2) of Transpore^{TM} tape was placed over a quartz cuvette; prepared formulations of 2 mg cm^{-2} were allowed to spread and adhere to transpore tape by an adhesive (caprolactam). Absorbance is then measured against a blank of transpore tape with the adhesive alone. An equivalent amount of the intact sunscreen oil was also tested for comparison. The intensity of radiation transmitted through the tape was determined automatically by recording the photocurrent in 5 nm steps from 290 to 400 nm using a double beam spectrophotometer (UV-1601, Shimadzu, Japan). For each formulation, the transmittance was determined and the monochromatic protection factors [PF(λ)] and their respective standard deviations [Δ P(λ)] were calculated. The SPF was predicted from the transmission measurements according to the following equation (Diffey and Robson, 1989):

$$\mathrm{SPE} = \sum_{290}^{400} E(\lambda)\varepsilon(\lambda) \Big/ \sum_{290}^{400} E(\lambda)\varepsilon(\lambda)/\mathrm{PF}(\lambda),$$

where $E(\lambda)$ is the spectral irradiance of terrestrial sunlight under defined conditions and $\varepsilon(\lambda)$ is the relative effectiveness of UV radiation at wavelength λ in producing delayed erythema in human skin (the so-called erythema action spectrum). The values of $E(\lambda)$ used were derived from the published data (Diffey and Robson, 1989). The erythema action spectrum used in the calculation was adopted by the International Commission on Illumination (CIE) as a ''reference action spectrum'' (Mckinlay and Diffey, 1987). Data were determined from the average of three determinations.

Testing for photostability

A series of beakers (one beaker (35 × 42 mm) for each time interval) containing a constant weight of microspheres in addition to a beaker containing the intact oil as reference were introduced in a UV cabinet and irradiated by means of a UV lamp (Phillips 8V, 285–320 nm). The lamp was calibrated against Eldomet Dosimeter 081 (Germany) (Nour et al., 2006; Tursilli et al., 2006). The intensity used in the experiments was 1450 Dw cm^{-2}. The distance from the source to the microspheres was 6 cm. Beakers were removed from the cabinet sequentially at selected time intervals. The microspheres were crushed by grinding; the oil was dissolved in methanol and assayed by HPLC. Each experiment was done in triplicate. Percent protection was calculated according to the following equation:

% protection
= 100 − (concentration of degradation product in formula after exposure)/(concentration of degradation product in e)

HPLC analysis

A Novpack-ODS C_{18} column (150 mm × 3.9 mm); particle size 4 μm was used for the analysis. The mobile phase was prepared by mixing methanol and water in a ratio of 85:15 by volume. The solvent was allowed to equilibrate, to be degassed and the column was conditioned for at least 30 min before injection. The samples were filtered using 0.45 μm filter before use. The flow rate was 1.0 mL min^{-1}. All measurements were performed using UV visible detector at a wavelength of 310 nm at an ambient temperature.

Validation of the HPLC method

Assay validation of the proposed HPLC method for the analysis of OMC

Linearity. Aliquots equivalent to 1–8 μg of OMC were accurately transferred from their working solutions (0.01 mg mL^{-1} in methanol) into a series of 10-mL volumetric flasks, and the volume was completed with methanol. 10 μl in triplicate of each solution was injected to HPLC and the peak areas were recorded. Calibration curves were plotted representing the relationship between the recorded areas and the corresponding concentrations, then the regression equations were computed.

Accuracy. The accuracy of the method was assessed by the determination of different concentrations of OMC. The mean percentage accuracy is represented.

Precision. The repeatability (intraday) and intermediate precision (interday precision) were evaluated by assaying freshly prepared samples of OMC in triplicate in concentrations of 0.2, 0.3 and 0.4 μg mL^{-1} (in methanol) within one day and for three successive days. The intraday and the interday relative standard deviation (RSD) values obtained are represented.

Assay validation of the proposed HPLC method for determination of OMC and its degradation product

To assess the validity of the suggested method to accurately determine OMC in the presence of its photodegradation product, the peaks for OMC and degradation product were evaluated for resolution, tailing factor, relative retention time, column capacity, column efficiency and height equivalent to one theoretical plate (HETP).

Results and discussion

Physicochemical assessment of the microspheres

Flowability testing

The cw microspheres were superior to bw analogues in flowability indices at both tested ratios. Better consolidation properties of cw might protect neighbouring microspheres from sticking to each other rendering them more flowable. On the other hand, it was noticed that microspheres of both waxes at the ratio of 2:1 were less flowable (Table 1) than those at ratios 4:1. This could be interpreted on the basis of particle size analysis (Figure 2, Table 1), which showed a shifting towards smaller size ranges for microspheres of ratio 2:1. This was in agreement with the cohesion theory (Wells, 1988), which stated that finer particles with higher surface to mass ratios are more cohesive than coarser particles. As cohesive force between neighbouring particles increases, it opposes the flow of particles, being stronger than gravitational stress.

Table 1. Physico-chemical assessment of the tested microspheres.

	Microsphere type			
	cw		bw	
	2:1*	4:1*	2:1*	4:1*
Flowability indices				
Angle of repose	35.1	33.9	44.0	35.3
Carr's index	20.0	4.4	25.0	15.0
Hausner ratio	1.3	1.1	1.3	1.2
Particle size analysis (μm)				
Mean	3.8	6.5	4.1	6.5
Mode	3–5	5–7	3–5	3–5
Max	6.3	14.1	5.9	12.9
Min	1.3	3.3	2.1	3.4
Oil content (%)	96.7	98.7	97.4	98.6
SPF†	5.8	11.0	1.7	1.5

Notes: *Wax to drug ratio.
†SPF values of the pure oil in an amount equivalent to that present in microspheres in ratios 2:1 and 4:1 were found to be 11.8 and 11.9, respectively.

Evaluation of encapsulation efficiency

Table 1 shows high values of oil content for all tested microspheres with a mean value of 97.8% ± 0.97 from the theoretical. The wax encapsulation method adopted thus succeeded in including most of the oil content inside the wax matrix.

Scanning electron microscopy

SEM analysis of the samples (representative example shown in Figure 1) revealed that all microspheres prepared were rather spherical in shape. In contrast to an obviously smooth surface shown by the 2:1 microspheres of both waxes, the surface of 4:1 ratio microspheres revealed greater roughness, which might be due to the nonuniform deposition of successive amount of wax.

Particle size analysis

Particle size histogram for both cw and bw microspheres (Figure 2) shows that microspheres containing double the amount of wax in their matrix (ratio 4:1) exhibited positive skewness towards the larger particle size range. It seemed that increasing the per cent of wax during the encapsulation process caused an increase in the viscosity of the internal phase of the emulsion. This might consequently increase the globule size resulting in about 10% and 16% of the microspheres yield (for cw and bw, respectively) in a larger size range (9–14 μm).

The mean particle size for all tested microspheres except those of bw at the ratio 4:1 lied in the modal size range (Table 1) which makes it beneficial for scaling up the formulae on industrial scale production.

Determination of SPF

SPF detected for bw microspheres was significantly lower than any cw formulation (Table 1). This could be attributed to the lower spreadability of the bw formulae onto the surface of the transpore tape. The decreased spreadability

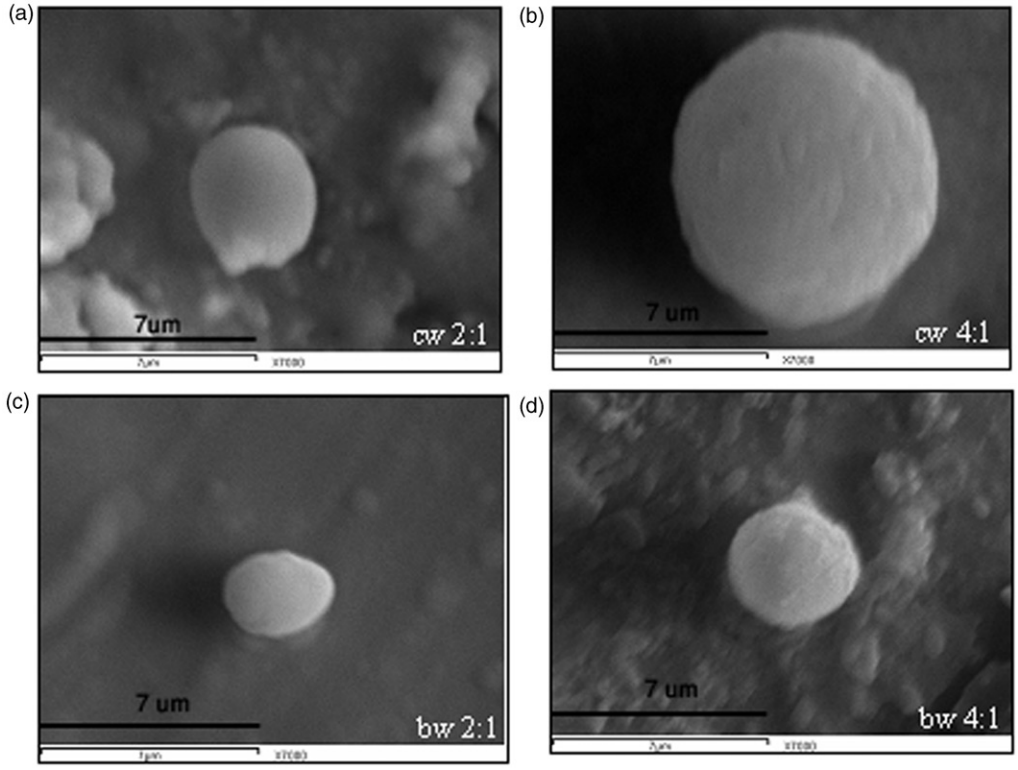

Figure 1. SEM images (magnification: 7000×) for the following polymer to drug ratios: (a) cw 2:1, (b) cw 4:1, (c) bw 2:1 and (d) bw 4:1.

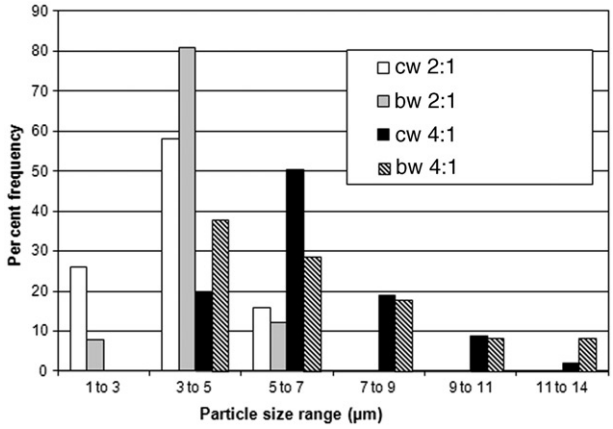

Figure 2. Particle size histogram of cw and bw microspheres.

Table 2. The per cent remaining intact oil after different times of UV exposure for the tested microspheres.

Time of UV exposure (min)	% Protection of the oil			
	cw		bw	
	2:1*	4:1*	2:1*	4:1*
30	91.8	93.7	93.3	92.2
60	88.0	87.9	88.5	86.3
90	88.7	85.9	84.7	82.9
150	87.8	82.2	83.9	82.3
180	83.0	81.8	81.1	80.4

Note: *Wax-to-drug ratio.

might be due the soft nature of the microspheres at ambient temperature rendering them sticky upon spreading. Thus, they did not properly cover the surface of the cuvette, allowing thereby increased transmission of UV radiation.

Comparing the SPF of cw 2:1 and 4:1 indicated that the 4:1 ratio (11.0) had a remarkably high value which was very close to that of the intact oil (11.9) in an amount equivalent to that present in the microspheres. The higher SPF detected is probably due to the appropriate coverage of the whole surface of the tape by cw microspheres (4:1). This may be on the one hand due to the greater flowability index of the formulation (Table 1) permitting a homogeneous distribution of the particles on the tape and on the other hand due to the presence of the microspheres in a wide particle size range (3.3–14.1) so that smaller particles could fill the interparticulate spaces.

Testing of photostability

The ability of the formulated microspheres to protect OMC from photodegradation is shown in Table 2. It was clear that the abilities of both waxes to protect OMC were similar to the tested formulae. Microspheres of both waxes at the two tested ratios gave a mean protection of 81.6% ± 1.1 after 3 h of exposure to UV. This result showed that the method of encapsulation adopted have succeeded to include most of the oil in the interior of the matrix of microspheres away from ambient light effects. The selection of the best formula for further clinical trials will be on the basis of the physical characterization of the prepared microspheres.

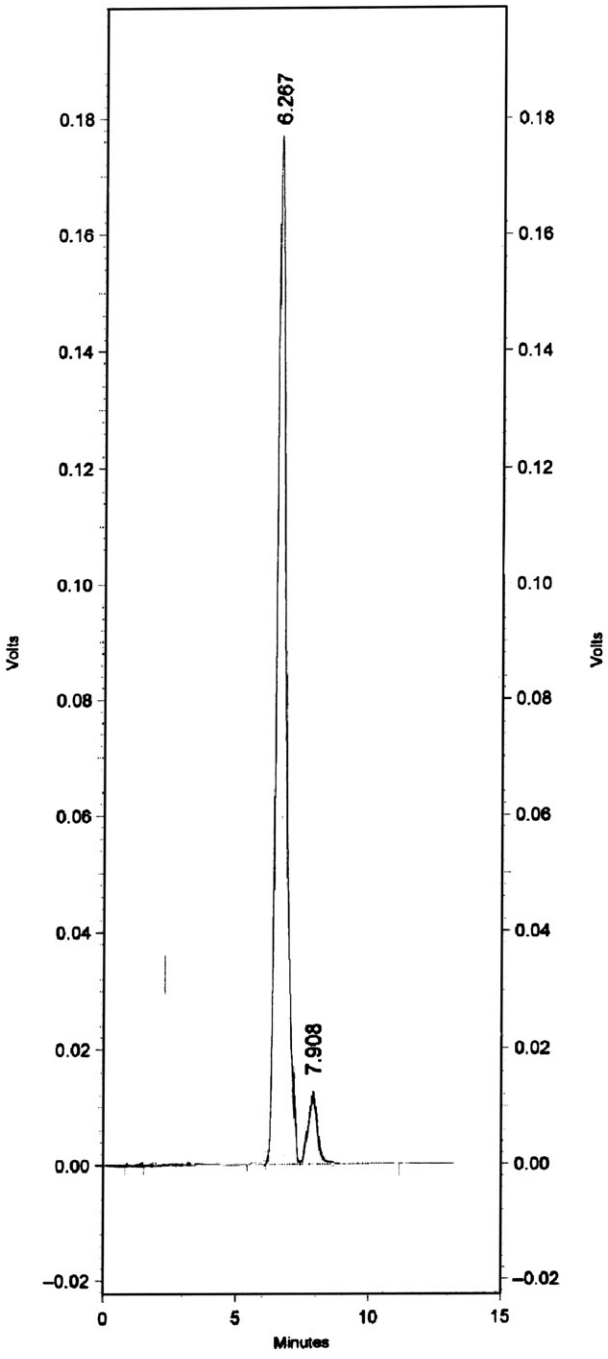

Figure 3. HPLC chromatogram for OMC (at 6.267 min) in the presence of its photodegradation (at 7.908 min).

Establishment of a HPLC analysis method for the determination of OMC and its degradation product

Different C_8 and C_{18} columns were tested for proper separation of the oil from its degradation product. It was found that Lichrosorbe C_{18} column allowed good separation of OMC from its degradation product, but the resulted peaks suffered from lack of symmetry and significant tailing. Best results were obtained by using Novpack C_{18} column (Figure 3).

Different mobile phases were tried for the chromatographic separation of the drug and its degradation product using column Novpack C_{18} including acetonitrile and water containing 10^{-3} M perchloric acid (5:95 v/v), methanol – tetrahydrofuran – water (4:6:6 v/v/v), and methanol – water (50:50 v/v) containing 0.1% triethylamine. Pure methanol was also tried. The most satisfactory separation was obtained using a mobile phase consisting of methanol – water (85:15 v/v). Different column lengths, 125 mm × 4 mm, 150 mm × 4.6 mm and 150 mm ×3.9 mm, were tested. The latter gave the best result for the separation. Working at a flow rate of 2 mL min^{-1} was optimum for separation.

Table 3. Results of assay validation of the proposed HPLC methods for the analysis of OMC.

Parameter	Proposed method
	OMC
Accuracy	
Mean ± RSD (%)	100.03 ± 1.04
Precision	
Repeatability (mean ± RSD, %)*	99.67 ± 0.42
Reproducibility (mean ± RSD, %)†	100.03 ± 0.24
Linearity	
Slope	15.46
SE of slope	0.25
Intercept	0.45
SE of intercept	0.12
Correlation coefficient	0.9992
Range (μg mL^{-1})	0.1–0.8

Notes: *The intraday ($n = 3$), average of three different concentrations repeated three times within the day.
†The interday of sample concentration 0.3 μg mL^{-1} repeated three times in three successive days.

HPLC method validation

Assay validation of the proposed HPLC method for the analysis of OMC

The validity of the proposed HPLC method for the analysis of OMC was assessed. Satisfactory results were obtained for linearity, accuracy and precision of the proposed method (Table 3).

Assay validation of the proposed HPLC method for determination of OMC and its degradation product

Results obtained for resolution, tailing factor, relative retention time, column capacity, column efficiency and HETP were all in the optimum range (Adamovics, 1997) for successful separation of OMC from its degradation product (Table 4).

Conclusion

OMC, which is known to suffer from photodegradation was successfully encapsulated into wax microspheres. All the tested formulae gave a satisfactory and similar protection after 180 min exposure to UV radiation. However, physicochemical characterization with respect to flowability,

Table 4. Parameters for system suitability test for the proposed HPLC method.

Parameter	Obtained values	Reference values* for optimum separation
Resolution (R)	$R_{1,2} = 1.673$	More than 1 for good resolution
Tailing factor (T)	$T_1 = 1.1 \quad T_2 \approx 1$	T = 1 for a typical symmetric peak
Relative retention time (α)	$\alpha_{1,2} = 1.26$	More than 1 for good separation
Column capacity (K)	$K_1 = 5.27 \quad K_2 = 6.91$	1–10 is acceptable
Column efficiency (N)	$N_1 = 501.4 \quad N_2 = 1419.8$	Increases with efficiency of separation
HETP	$HETP_1 = 0.011 \quad HETP_2 = 4.1 \times 10^{-3}$	The smaller the value the higher is the column

Notes: Subscripts 1 and 2 denote the peak of OMC and the peak of the degradation product, respectively.
*Adamovics (1997).

particle size distribution and SPF revealed the superiority of cw 4:1, which suggests the formula to be scaled up on industrial scale production, aiming to provide a dry method for the application of the oil with a high chemical stability. Furthermore, the method applied for the analysis of OMC and its degradation product was proven to be a satisfactory and valid method.

Declaration of interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of this article.

References

Adamovics JA, 1997. Chromatographic analysis of pharmaceuticals. New York, Basel, Hong Kong: Marcel Dekker, pp. 11–17.

Alvarez-Román R, Barré G, Guy RH, Fessi H. Biodegradable polymer nanocapsules containing a sunscreen agent: Preparation and photoprotection. Eur J Pharm Biopharm, 2001;52:191–5.

Aulton ME, 2007. Aulton's pharmaceutics: The design and manufacture of medicines. Philadelphia: Churchill Livingstone Elsevier, pp. 176–7.

Carstensen JT. 2001. Advanced pharmaceutical solids. New York, Basel: Marcel Dekker, pp. 302, 311.

Davis WL, Gloor WT. Batch production of pharmaceutical granulations in a fluidized bed I: Effects of process variables on physical properties of final granulation. J Pharm Sci, 1971;60(12):1869–74.

Diffey BL, Robson J. A new substrate to measure sunscreen protection factors throughout the ultraviolet spectrum. J Soc Cosmet Chem, 1989;40:127–33.

Gaspar LR, Maia Campos PMBG. Evaluation of the photostability of different UV filter combinations in a sunscreen. Int J Pharm, 2006;30:123–8.

Gaspar LR, Maia Campos PMBG. Photostability and efficacy studies of topical formulations containing UV filters combination and vitamins A, C and E. Int J Pharm, 2007;343:181–9.

Huong SP, Andrieu V, Reynier JP, Rocher E, Fourneron JD. The photoisomerization of the sunscreen ethylhexyl *p*-methoxy cinnamate and its influence on the sun protection factor. J Photochem Photobiol A: Chem, 2007;186:65–70.

Iannuccelli V, Sala N, Tursilli R, Coppi G, Scalia S. Influence of liposphere preparation on butyl-methoxydibenzoylmethane photostability. Eur J Pharm Biopharm, 2006;63:140–5.

Janjura NR, Mogensen B, Anderson AM, Peterson JH, Henriksen M, Shakkebaek NE, Wulf HC. Systemic absorption of the sunscreens benzophenone-3, octyl methoxycinnamate, and 3-(4-methylbenzylidene) camphor after whole body topical application and reproductive hormone levels in humans. J Invest Dermatol, 2004;123:57–61.

Kullavanijaya P, Lim HW. Photoprotection. J Am Acad Dermatol, 2005;52:937–58.

Mckinlay AF, Diffey BL. A reference action spectrum for ultraviolet induced erythema in human skin. CIE J, 1987;6:17–22.

Nour SA, El Gazayerly ON, Abdel Malak NS. 2006. A pharmaceutical study on novel cosmeceutical preparations containing antioxidants, Dissertation, Cairo University, Egypt.

Pattanaargson S, Limphong P. Stability of octyl methoxycinnamate and identification of its photo-degradation product. J Cosmet Sci, 2001;23:153–60.

Pattanaargson S, Munhapol T, Hirunsupachot P, Luangthongaram P. Photoisomerization of the octyl methoxycinnamate. J Photochem Photobiol A: Chem, 2004;161:269–74.

Perguini P, Simeoni S, Scalia S, Genta I, Modena T, Conti B, Pavanetto F. Effect of nanoparticle encapsulation on the photostability of the sunscreen agent, 2-ethylhexyl-p-methoxycinnamate. Int J Pharm, 2002;246:37–45.

Ramadan A, El Massik M, El Khordagui L, Daabis N, Hammouda Y. Surface treatment: A potential approach for enhancement of solid-state photostability. Int J Pharm, 2006;307:141–9.

Scalia S, Tursilli R, Sala N, Iannucelli V. Encapsulation in lipospheres of the complex between butyl methoxydibenzoylmethane and hydroxypropyl-β-cyclodextrin. Int J Pharm, 2006;320:79–85.

Sinko PJ, 2006. Martin's physical pharmacy and pharmaceutical sciences. Philadelphia: Lippincott Williams and Wilkins, p. 558.

Tursilli R, Casolari A, Iannuccelli V, Scalia S. Enhancement of melatonin photostability by encapsulation in lipospheres. J Pharm Biomed Anal, 2006;40:910–14.

Tursilli R, Piel G, Delattre L, Scalia S. Solid lipid microparticles containing the sunscreen agent octyl-dimethylaminobenzoate: Effect of the vehicle. Eur J Pharm Biopharm, 2007;66:483–7.

Wells J, 1988. Pharmaceutical preformulation. The physicochemical properties of drug substances. UK: Ellis Horwood Limited, pp. 209–210.

Westesen K, Siekmann B. 1996. Microencapsulation. In: Bonita S, ed. Methods and industrial applications. New York, Basel: Marcel Dekker, pp. 214–7, 232.

Wissing SA, Müller RH. The development of an improved carrier system for sunscreen formulations based on crystalline lipid nanoparticles. Int J Pharm, 2002;242:373–5.