UNIVERSITI PUTRA MALAYSIA

DESIGN AND OPTIMISATION OF FULLERENE-BASED NANOEMULSION SYSTEM FOR NANOCOSMECEUTICAL APPLICATIONS

NGAN CHENG LOONG

DESIGN AND OPTIMISATION OF FULLERENE-BASED NANOEMULSION SYSTEM FOR NANOCOSMECEUTICAL APPLICATIONS

By

NGAN CHENG LOONG

Thesis Submitted to the School of Graduate Studies, Universiti Putra Malaysia, in Fulfilment of the Requirements for the Degree of Doctor of Philosophy

June 2015

Abstract of the thesis presented to the Senate of Universiti Putra Malaysia in the fulfilment of the requirement for the degree of Doctor of Philosophy

DESIGN AND OPTIMISATION OF FULLERENE-BASED NANOEMULSION SYSTEM FOR NANOCOSMECEUTICAL APPLICATIONS

By

NGAN CHENG LOONG

June 2015

Chairman : Professor Mahiran Basri, PhD
Faculty : Science

Fullerene is gaining interest as an antioxidant in the cosmetic industry but the primary challenges are the incorporation of fullerene due to its hydrophobicity and difficulties in formulating a stable carrier system. Newly developed nanoemulsion system was designed specifically for transdermal application in cosmeceutical applications. Pseudoternary phase diagrams were constructed to serve as platform in building an emulsion system which constituted of palm kernel oil esters (PKOEs), non-ionic surfactant(s), water and fullerene as bioactive ingredient. Non-ionic surfactants applied were polyoxyethylene sorbitan monooleate (Tween 80) and sorbitan monooleate (Span 80) with different mixed surfactant ratios (MSRs). Based on the results, binary surfactant system of Tween 80:Span 80 with MSR of 8:2 performed better in emulsification capability by exhibiting larger monophasic region compared to the usage of single surfactant. The hydrophilic-lipophilic balance value of mixed surfactant unveiled the largest homogeneous and isotropic regions is 12.86.

Compositions selected from pseudoternary phase diagrams were designated as pre-formulation. Excipients contained alongside within the formulation include xanthan gum as rheology modifier, beeswax as emollient and phenonip as anti-microbial agent. Nanoemulsions were prepared by high shear homogeniser, followed by ultrasonic cavitation. The physicochemical behaviours of formulations with various proportions of components were extensively characterised. Essentially, the mean particle size was in the nano-size range of 70-160 nm. It was found that xanthan gum amount with 0.60% (w/w) or higher was able to stabilise the emulsion droplets by forming polymer network with steric stabilising effect.

The effect of composition on nanoemulsion; PKOEs, surfactants and xanthan gum amount on variation of particle size, ζ-potential and viscosity were investigated. Multivariate statistical techniques such as response surface

methodology (RSM), Box-Behnken (BBD) and central composite rotatable (CCRD) designs were used to optimise the formulation in acquiring desirable properties of nanoemulsion system. The optimum formulation comprised 12.50% of PKOEs, 7.68% of Tween 80:Span 80 (4:1) and 0.90% of xanthan gum yielded a particle size, ζ-potential and viscosity of 153.6 nm, −53.4 mV and 42.1 Pa s, respectively. Linear relationships were observed in all cases where no interaction occurred between the variables. According to the pareto graphic analysis, surfactant amount gave the largest effect on particle size and ζ-potential whereas viscosity was largely dependent on xanthan gum amount.

Second stage of optimisation was performed to discover the influence of process parameters on the similar responses as investigated earlier. The effect of process types on response variables was complex being dependent on the existence of interaction between the parameters (quadratic polynomial model). The results showed that nanoemulsion prepared under homogenisation rate of 4352 rpm and sonication amplitude of 48% for 97 s would produce particle size, ζ-potential and viscosity of 152.5 nm, −52.6 mV and 44.6 Pa s, respectively. Interestingly, in both optimisation designs, CCRD demonstrated excellent model fitting and estimation of actual values than BBD with lower residual standard error. Nonetheless, both designs predicted similar responses which affirmed one another in terms of reliability to obtain optimum formulation with improved attributes.

Rheological behaviour of nanoemulsion was evaluated using viscometry test. From the rheograms, nanoemulsion exhibited shear thinning (pseudoplastic) behaviour which obeys the power law model. The results from oscillatory strain sweep test showed the wide linear viscoelastic region which directly correlated to high rigidity of the system. The architecture of the nanoemulsion system was analysed using transmission electron microscope to study the morphology. The micrographs showed that the particle size was in agreement with the measured size. In the physical stability and thermal stress test, the optimum formulation was stable under high centrifugal force, storage at room temperature and 45°C for 90 days while maintaining its nano-sized particle and high ζ-potential with texture and consistency being preserved. Likewise, the colloidal system was able to withstand freeze-thaw cycles and having low rate of Ostwald ripening.

In the safety evaluation test, nanoemulsion showed no cytotoxicity effect on fibroblast cell (3T3) up to 48 hours. Results also showed that nanoemulsion was non-irritant with Human Irritancy Equivalent (HIE) scores of 0.36. *In vivo* biophysical attributes of skin studies showed that the skin hydration increased without any increase in transepidermal water loss up to 28 days of the treatment period. However, with this finding, the skin hydration increased more progressively on application of fullerene-laden formulation compared to placebo (without fullerene). Collagen content was increased significantly which lead to improved water binding capacity. No visible skin reactions caused by dermal irritation, contact sensitisation or rash were experienced by the subjects during the treatment. This work concluded that a stable fullerene nanoemulsion fits for cosmetic was successfully developed and showed potential collagen regeneration in human skin.

Abstrak tesis dikemukakan kepada Senat Universiti Putra Malaysia sebagai memenuhi keperluan untuk ijazah Doktor Falsafah

REKABENTUK DAN PENGOPTIMUMAN FULERENA BERASASKAN SISTEM NANOEMULSI BAGI KEGUNAAN NANOKOSMESEUTIKAL

Oleh

NGAN CHENG LOONG

Jun 2015

Pengerusi : Profesor Mahiran Basri, PhD
Fakulti : Sains

Fulerena semakin mendapat perhatian sebagai antioksidan dalam industri kosmetik tetapi cabaran utama adalah penggabungan fulerena kerana kehidrofobikannya dan kesukaran untuk memformulasikan sebuah sistem pembawa yang stabil. Sistem nanoemulsi baru telah dicipta khusus untuk aplikasi transdermal sebagai formulasi kosmeseutikal. Gambar rajah tiga fasa telah dibina sebagai platfom dalam pembinaan sistem emulsi yang terdiri daripada ester minyak isirong sawit (PKOEs), surfaktan bukan ion, air dan fulerena sebagai bahan bioaktif. Surfaktan bukan ion yang digunakan adalah polioksietilena sorbitan monooleat (Tween 80) dan sorbitan monooleat (Span 80) pada nisbah campuran surfaktan (MSRs) yang berbeza. Hasil keputusan menujukkan sistem binari surfaktan bagi nisbah Tween 80:Span 80 dengan nilai MSR 8:2 mempunyai keupayaan pengemulsian yang lebih baik dengan menghasilkan kawasan monofasik yang lebih besar berbanding dengan penggunaan surfaktan tunggal. Nilai keseimbangan hidrofilik-lipofilik bagi campuran surfaktan yang menghasilkan kawasan homogen dan isotropik terbesar adalah 12.86.

Komposisi yang dipilih daripada gambar rajah tiga fasa kemudian digunakan sebagai pra-formulasi. Bahan-bahan lain yang terkandung dalam formulasi termasuk gam xantan sebagai pengubahsuai reologi, lilin lebah sebagai emolien dan phenonip sebagai agen anti-mikrob. Nanoemulsi telah disediakan dengan menggunakan homogeniser ricih tinggi dan diikuti oleh peronggaan ultrasonik. Ciri-ciri fizikokimia bagi formulasi dengan pelbagai bahagian terhadap komposisi telah ditentukan secara mendalam. Secara umumnya, purata saiz zarah adalah dalam julat 70-160 nm dalam saiz nano. Gam xantan sebanyak 0.60% (w/w) atau lebih didapati mumpunyai kebolehan untuk menstabilkan titisan emulsi dengan pembentukan jaringan polimer terhadap kesan pengstabilan sterik.

Kesan kandungan PKOEs, surfaktan dan gam xantan terhadap perubahan saiz zarah, keupayaan ζ dan kelikatan telah disiasat. Teknik statistik multivariat seperti kaedah gerak balas permukaan, rekabentuk Box-Behnken (BBD) dan komposit pusat berputar (CCRD) telah digunakan untuk mengoptimumkan formulasi dalam mencapai sistem nanoemulsi yang diingini. Formulasi optimum terdiri daripada 12.50% PKOEs, 7.68% Tween 80:Span 80 (4:1) dan 0.90% gam xantan telah menghasilkan saiz zarah, keupayaan ζ dan kelikatan sebanyak 153.6 nm, -53,4 mV, dan 42.1 Pa s masing-masing. Hubungan linear telah dapat diperhatikan dalam semua kes di mana tidak ada saling tindakan berlaku antara pembolehubah-pembolehubah. Menurut analisis pareto grafik, jumlah surfaktan telah memberi kesan yang terbesar kepada saiz zarah dan keupayaan ζ manakala kelikatan adalah sangat bergantung kepada kandungan gam xantan.

Pengoptimuman peringkat kedua dilakukan untuk mengetahui kesan bagi proses parameter terhadap gerak balas yang telah disiasat sebelum ini. Kesan bagi jenis proses pada pembolehubah respon adalah kompleks bergantung kepada kewujudan saling tindakan antara parameter (model polinomial kuadratik). Hasil kajian menunjukkan bahawa nanoemulsi yang disediakan pada kadar homogenisasi 4352 rpm dan sonikasi amplitud 48% selama 97 s akan menghasilkan saiz zarah, keupayaan ζ dan kelikatan 152.5 nm, -52,6 mV dan 44.6 Pa s masing-masing. Dalam kedua-dua rekabentuk pengoptimuman, CCRD menunjukkan model yang lebih baik bersesuaian dengan anggaran nilai sebenar berbanding BBD dengan ralat piawai residu yang lebih rendah. Walau bagaimanapun, kedua-dua rekabentuk telah diramalkan mempunyai gerak balas yang sama yang disahkan di antara satu sama lain dari segi reliabiliti untuk mendapatkan formulasi yang optimum dengan sifat-sifat yang telah ditingkatkan.

Ciri reologi nanoemulsi telah ditentukan menggunakan ujian kelikatan. Daripada reogram, nanoemulsi mempamerkan sifat ricih penipisan (pseudoplastik) yang mematuhi model 'power law'. Hasil daripada ujian ketegangan ayunan menunjukkan rantau linear viskoelastik yang luas yang berkadar terus dengan sistem ketegaran yang tinggi. Struktur sistem nanoemulsi telah dianalisis dengan menggunakan mikroskop elektron transmisi bagi mengkaji morfologinya. Mikrograf menunjukkan bahawa saiz zarah adalah bersesuaian dengan saiz yang diukur. Dalam ujian kestabilan fizikal dan tekanan haba, formulasi optimum didapati stabil di bawah daya empar tinggi pada suhu bilik dan 45℃ selama 90 hari di samping mengekalkan zarah bersaiz nano dan keupayaan ζ yang tinggi dengan tekstur dan konsistensi yang dapat dikekalkan. Sistem koloid mampu menahan kitaran beku-cair dan mempunyai kadar 'Ostwald ripening' yang rendah.

Dalam ujian penilaian keselamatan, nanoemulsi tidak memberi kesan sitotoksiti pada sel fibroblast (3T3) sehingga 48 jam. Keputusan juga menunjukkan bahawa nanoemulsi adalah tidak merengsa dengan skor 'Human Irritancy Equivalent' (HIE) pada 0.36. Kajian *in vivo* sifat biofizikal kulit menunjukkan bahawa penghidratan kulit meningkat tanpa sebarang kenaikan kehilangan

transepidermal air sehingga 28 hari dalam tempoh rawatan. Walau bagaimanapun, penghidratan kulit meningkat dengan lebih progresif dalam penggunaan fulerena berbanding dengan plasebo (tanpa fulerena). Kandungan kolagen telah meningkat dengan ketara yang membawa kepada kapasiti pengikatan air yang lebih baik. Sepanjang tempoh rawatan, kesan tindak balas pada kulit yang berpunca daripada kerengsaan kulit sensitif terhadap sentuhan atau ruam yang dialami oleh subjek tidak kelihatan. Kajian ini merumuskan bahawa nanoemulsi fulerena yang stabil dan sesuai untuk kosmetik telah berjaya dicipta serta menunjukkan potensi pertumbuhan semula kolagen dalam kulit manusia.

ACKNOWLEDGEMENTS

First and above all, I praise God for the successful completion of my research. I would like to express my deepest and sincere appreciation to my supervisor, Prof. Dr. Mahiran Basri for her invaluable guidance, consistent support and encouragement throughout the course of this research. It has indeed been an honour and privilege to conduct this research under your supervision. My appreciation also goes to members of my supervisory committee, Dr. Roghayeh Abedi Karjiban, Dr. Emilia Abdul Malek and Dr. Minaketan Tripathy for their strong support, constructive comments and guidance during the meeting.

A special thanks to my research members, Dr. Hamid Reza Fard Masoumi, Lim Chaw Jiang, Ng Sook Han, Siti Hajar Musa and my labmates from the Research Laboratory of Chemical Synthesis 105, Faculty of Science, for their support, encouragement and sharing all these while; Ikhwan Hadi and my friends from the Laboratory of Fundamentals of Pharmaceutics, Faculty of Pharmacy, UiTM for their warm welcome and assistance in my early research. My sincere appreciation is extended to Ms Norhayati Yusuf from Laboratory of Molecular Biomedicine, Institute of Bioscience (IBS) for her assistance in the operation of the instruments.

I would like to acknowledge the Ministry of Education (MOE) for their generous financial support in the form of MyPhD, under MyBRAIN 15 and the research grant allocation which aided me in the completion of my study. My heartfelt appreciation extends to all lecturers and management staffs in the Department of Chemistry, Universiti Putra Malaysia for their assistance in my research work.

Last but not least, I would like to thank my beloved parents and brothers from the bottom of my heart for their unceasing love, patience, support, encouragement and understanding. Words cannot express how grateful I am for their care and concern for me especially in regards to my health and well-being. I am also particularly grateful to Christine and her family for their unwavering support and prayers throughout the course of my research. I love you.

This thesis was submitted to the Senate of Universiti Putra Malaysia has been accepted as fulfilment of the requirements for the degree of Doctor of Philosophy. The members of Supervisory Committee were as follows:

Mahiran binti Basri, PhD
Professor
Faculty of Science
Universiti Putra Malaysia
(Chairman)

Roghayeh Abedi Karjiban, PhD
Senior Lecturer
Faculty of Science
Universiti Putra Malaysia
(Member)

Emilia binti Abdul Malek, PhD
Senior Lecturer
Faculty of Science
Universiti Putra Malaysia
(Member)

Minaketan Tripathy, PhD
Senior Lecturer
Faculty of Pharmacy
Universiti Teknologi MARA
(Member)

BUJANG KIM HUAT, PhD
Professor and Dean
School of Graduate Studies
Universiti Putra Malaysia

Date:

Declaration by graduate student

I hereby confirm that:

- this thesis is my original work;
- quotations, illustrations and citations have been duly referenced;
- this thesis has not been submitted previously or concurrently for any other degree at any other institutions;
- intellectual property from the thesis and copyright of thesis are fully-owned by Universiti Putra Malaysia, as according to the Universiti Putra Malaysia (Research) Rules 2012;
- written permission must be obtained from supervisor and the office of Deputy Vice-Chancellor (Research and Innovation) before thesis is published (in the form of written, printed or in electronic form) including books, journals, modules, proceedings, popular writings, seminar papers, manuscripts, posters, reports, lecture notes, learning modules or any other materials as stated in the Universiti Putra Malaysia (Research) Rules 2012;
- there is no plagiarism or data falsification/fabrication in the thesis, and scholarly integrity is upheld as according to the Universiti Putra Malaysia (Graduate Studies) Rules 2003 (Revision 2012-2013) and the Universiti Putra Malaysia (Research) Rules 2012. The thesis has undergone plagiarism detection software.

Signature: ______________________ Date : ________________

Name and Matric No.: Ngan Cheng Loong, GS30141

Declaration by Members of Supervisory Committee

This is to confirm that:

- the research conducted and the writing of this thesis was under our supervision;
- supervision responsibilities as stated in the Universiti Putra Malaysia (Graduate Studies) Rules 2003 (Revision 2012-2013) are adhered to.

Signature : ______________________________
Name of Chairman of Supervisory Committee : Mahiran binti Basri, PhD

Signature : ______________________________
Name of Member of Supervisory Committee : Roghayeh Abedi Karjiban, PhD

Signature : ______________________________
Name of Member of Supervisory Committee : Emilia binti Abdul Malek, PhD

Signature : ______________________________
Name of Member of Supervisory Committee : Minaketan Tripathy, PhD

TABLE OF CONTENTS

LIST OF ABBREVIATIONS

3D	three dimensional
BBD	Box-Behnken design
c.u.	corneometric unit
CCRD	central composite rotatable design
CIR	Cosmetic Ingredient Review
DMEM	Dulbecco's Modified Eagle Medium
FDA	Food and Drug Administration
HLB	hydrophilic-lipophilic balance
LCFS	lipid formulation classification system
LVR	linear viscoelastic region
MSRs	mixed surfactant ratios
MTT	3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide
O/W	oil-in-water
OD	optical density
PKOEs	palm kernel oil esters
ROS	reactive oxygen species
rpm	revolutions per minute
RSE	residual standard error
RSM	response surface methodology
TEM	transmission electron microscopy
TEWL	transepidermal water loss
UV	ultraviolet
W/O	water-in-oil
w/w	weight per weight

CHAPTER 1

INTRODUCTION

Background of Study

So long as the desire to seek ultimate beauty, eternalise youthful appearance and revitalise skin wellness is instilled in oneself, demands for new effective and innovative skincare products in the market will continue to soar. Since then, the term "cosmeceutical" is often used in the cosmetic industry which has been classified as cosmetic products which yield therapeutic or medicinal benefits (Choi and Berson, 2006). Similarly to cosmetics, cosmeceuticals are applied topically but vary in which they contain bioactive compounds that can influence the biological function of skin and deliver nutrients to enhance skin health (Brandt *et al.*, 2011).

Cosmeceutical products show promising prospect which is highlighted by the substantial market growth in the coming years. According to the insight report, it forecasted the global cosmeceutical market, which is dominated by top European countries (United Kingdom, Germany, France, Italy and Spain) with 65% of the worldwide market, followed by United States and Japan, will reach US $42.4 billion by 2018 (GBI Research, 2013). Even so, massive cosmeceutical products are not strictly regulated and often times, consumers are deceived by the fascinating claims in the product information which is not scientifically proven or backed by rigorous clinical studies (Brandt *et al.*, 2011). As a matter of fact, efficacy of a cosmeceutical product is largely dependent on the bioavailability of bioactive compounds used in the formulations.

In order to improve the bioavailability on human skin, increase in penetration of bioactive compounds into human skin is undoubtedly necessary. Manufacturers of cosmetic products have recently shown increasing preference for multifunctional products in which different active agents can be incorporated to improve bioavailability and decrease side effect or toxicity due to lower active agent content. Recent advanced in nanotechnology and engineering proves to be effective in surging innovative formulations and product solutions. Novel strategies for skin delivery systems in cosmeceutical include vesicular systems, particulate systems, fibrous matrices and emulsion systems (Golubovic-Liakopoulos *et al.*, 2011).

A new generation hybrid of nanotechnology and emulsion technology is able to manipulate the delivery of bioactive compounds in achieving the best outcome of the treatment. Nanoemulsions are able to ensure these terms. Various bioactive compounds incorporated in nanoemulsions for application in the treatment for rheumatoid arthritis (Salim *et al.*, 2012) and medicinal research for inflammatory disorder (Peng *et al.*, 2010), have shown enhanced penetration of drugs. Nanoemulsions have also been developed for waterinsoluble active ingredients such as tocotrienol (Han *et al.*, 2011) and kojic acid dipalmitate (Al-Edresi and Baie, 2010) as cosmetic delivery system. Eventually, this comes down to the competency of the bioactive compounds and their purported biological activity.

Fullerene, being the third carbon allotrope, has been explored and deployed dynamically in the cosmeceutical industry on account of its excellent antioxidant activity (Lens, 2009). Fullerene and its derivatives are proven far better than α-tocopherol in term of antioxidant activity (Takada *et al.*, 2006; Wang *et al.*, 1999). Application of fullerenes in cosmeceutical has always been a challenge for the researchers due to their immiscibility in the water (Cataldo, 2008). Hence, some have been formulated where fullerenes are dissolved in squalane (Kato *et al.*, 2010a) and encapsulation of fullerenes in polyvinylpyrolidone (Xiao *et al.*, 2007) for cosmetic applications. However, there is limited information on the development of stable nanoemulsion systems for pristine fullerene.

Surfactants play an important role in acquiring a stable emulsion without any occurrence of sedimentation or flocculation over time. Ionic surfactants are not suitable for human use because they are easily affected by pH and change in ionic strength. Nevertheless, nanoemulsions with low surfactant concentration in the formulation could reduce any adverse toxicological and dermatological effects to human body (Han *et al.*, 2011). For high skin-compatibility cosmetic purposes, non-ionic surfactants are being used, namely Tween 80 and Span 80 with non-toxic and biocompatible (Azeem *et al.*, 2009), and vegetable oil, palm kernel oil esters (PKOEs) which show non-irritancy and increase in skin hydration (Keng *et al.*, 2009), would be suitable candidates in cosmetic formulations for skin rejuvenation.

In this study, palm-based colloidal systems were developed from the pseudoternary phase diagrams. Palm kernel oil esters are specialty esters which were chosen to be added into the formulation due to their excellent moisturising effect and wetting behaviour. Apart from its goodness and pure cosmeceutical benefit richness, development of palm-based products in Malaysia also serve as an initiative to promote market expansion of palm oil globally. Tween 80 and Span 80 were selected due to their high degree of compatibility with other ingredients, good chemical stability and low toxicity. Xanthan gum and beeswax are natural adjuvants added as rheological modifier and moisturiser, respectively to enhance the skin benefits and properties of the formulation. For longer shelf life purpose, a very low amount of phenonip was added as preservative. Formulations were developed after the suitable compositions were determined by using high-energy emulsification method to produce nanoemulsion systems. The potential of the nanoemulsion formulations were then evaluated on its safety and clinical trial on human skin.

Research Problems

Fullerene is well established for its antioxidant activity in various fields especially in cosmeceutical industries. Human skin has the water content of 10−20%, while more than 40% of bioactive materials used in the pharmaceutical and cosmetic industries are poorly water soluble (Tal-Figiel and Figiel, 2008), thus causes failure in delivery of bioactive compounds into human skin. Unfortunately, fullerene is hydrophobic in nature. Surface modification of fullerene has been done to increase its solubility in water but original activity of fullerene will be affected. Hence, a novel biocompatible delivery system is required to deliver fullerene to the human skin.

Like any other colloidal systems, nanoemulsion is prone to numerous types of physical instabilities. In fact, the greatest challenge is to maintain the particle size in nanometer range while remain physically stable for a period of time. The right compositions of each component and techniques in the preparation of formulation would be crucial to acquire such sophisticated colloidal system. This process is tedious and time-consuming to find the best formulation if the formulator was to consider the effect of each component individually. Besides, the potential of fullerene in collagen regeneration is still unknown.

Research Objectives

The specific objectives of this work are:

(i) To develop biocompatible palm kernel-based nanoemulsion systems incorporated with fullerene for transdermal applications.
(ii) To characterise the physicochemical, rheological properties and stability of the newly developed nanoemulsions.
(iii) To conduct optimisation of the formulation composition and process of the developed nanoemulsions.
(iv) To evaluate the safety of nanoemulsions and their biophysical attributes of human skin.

REFERENCES

Acharya, A., Moulik, S.P., Sanyal, S.K., Mishra, B.K., Puri, P.M., 2002. Physicochemical investigations of microemulsification of coconut oil and water using polyoxyethylene 2-cetyl ether (Brij 52) and isopropanol or ethanol. Journal of Colloid and Interface Science 245, 163-170.

Al-Edresi, S., Baie, S., 2010. *In-vitro* and *in-vivo* evaluation of a photo-protective kojic dipalmitate loaded into nano-creams. Asian Journal of Pharmaceutical Sciences 5, 251-265.

Ali, S.S., Hardt, J.I., Dugan, L.L., 2008. SOD activity of carboxyfullerenes predicts their neuroprotective efficacy: a structure-activity study. Nanomedicine: Nanotechnology, Biology and Medicine 4, 283-294.

Andersen, F.A., 2008. Final amended report on the safety assessment of methylparaben, ethylparaben, propylparaben, isopropylparaben, butylparaben, isobutylparaben, and benzylparaben as used in cosmetic products. International Journal of Toxicology 27, 1-82.

Anton, N., Benoit, J.-P., Saulnier, P., 2008. Design and production of nanoparticles formulated from nano-emulsion templates – A review. Journal of Controlled Release 128, 185-199.

Aoshima, H., Kokubo, K., Shirakawa, S., Ito, M., Yamana, S., Oshima, T., 2009a. Antimicrobial activity of fullerenes and their hydroxylated derivatives. Biocontrol Science 14, 69-72.

Aoshima, H., Saitoh, Y., Ito, S., Yamana, S., Miwa, N., 2009b. Safety evaluation of highly purified fullerenes (HPFs): based on screening of eye and skin damage. The Journal of Toxicological Sciences 34, 555-562.

Azeem, A., Rizwan, M., Ahmad, F.J., Iqbal, Z., Khar, R.K., Aqil, M., Talegaonkar, S., 2009. Nanoemulsion components screening and selection: a technical note. AAPS PharmSciTech 10, 69-76.

Baati, T., Bourasset, F., Gharbi, N., Njim, L., Abderrabba, M., Kerkeni, A., Szwarc, H., Moussa, F., 2012. The prolongation of the lifespan of rats by repeated oral administration of fullerene. Biomaterials 33, 4936-4946.

Baldwin, H.E., 2006. Cosmeceuticals in dermatology, Skin and Aging, p. 10.

Baroni, A., Buommino, E., De Gregorio, V., Ruocco, E., Ruocco, V., Wolf, R., 2012. Structure and function of the epidermis related to barrier properties. Clinics in Dermatology 30, 257-262.

Belo, S.E.D., Gaspar, L.R., Campos, P.M.B.G.M., 2011. Photoprotective effects of topical formulations containing a combination of *ginkgo biloba* and green tea extracts. Phytotherapy Research 25, 1854-1860.

Bergfeld, W.F., Belsito, D.V., Marks, J.G., Jr., Andersen, F.A., 2005. Safety of ingredients used in cosmetics. Journal of the American Academy of Dermatology 52, 125-132.

Binner, E.R., Robinson, J.P., Kingman, S.W., Lester, E.H., Azzopardi, B.J., Dimitrakis, G., Briggs, J., 2013. Separation of oil/water emulsions in continuous flow using microwave heating. Energy & Fuels 27, 3173-3178.

Bissett, D.L., 2009. Common cosmeceuticals. Clinics in Dermatology 27, 435-445.

Bontell, I., Häggblom, A., Bratt, G., Albert, J., Sönnerborg, A., 2013. Trends in antiretroviral therapy and prevalence of HIV drug resistance mutations in Sweden 1997–2011. PloS One 8, e59337.

Borse, M., Sharma, V., Aswal, V.K., Goyal, P.S., Devi, S., 2006. Aggregation properties of mixed surfactant systems of dimeric butane-1,4-bis(dodecylhydroxyethylmethylammonium bromide) and its monomeric counterpart. Colloids and Surfaces A: Physicochemical and Engineering Aspects 287, 163-169.

Bosi, S., Da Ros, T., Spalluto, G., Prato, M., 2003. Fullerene derivatives: an attractive tool for biological applications. European Journal of Medicinal Chemistry 38, 913-923.

Bouchemal, K., Briançon, S., Perrier, E., Fessi, H., 2004. Nano-emulsion formulation using spontaneous emulsification: solvent, oil and surfactant optimisation. International Journal of Pharmaceutics 280, 241-251.

Brandt, F.S., Cazzaniga, A., Hann, M., 2011. Cosmeceuticals: current trends and market analysis, Seminars in Cutaneous Medicine and Surgery. WB Saunders, pp. 141-143.

Burlando, B., Cornara, L., 2013. Honey in dermatology and skin care: a review. Journal of Cosmetic Dermatology 12, 306-313.

Cataldo, F., 2008. Solubility of fullerenes in fatty acids esters: a new way to deliver in vivo fullerenes. Theoretical calculations and experimental results, Medicinal Chemistry and Pharmacological Potential of Fullerenes and Carbon Nanotubes. Springer, pp. 317-335.

Chawla, P., Chawla, V., Maheshwari, R., A Saraf, S., K Saraf, S., 2010. Fullerenes: from carbon to nanomedicine. Mini Reviews in Medicinal Chemistry 10, 662-677.

Chen, F.F., Keasling, J.D., Tang, Y.J., 2013a. Bioremediation of nanomaterials. Google Patents.

Chen, L., Han, L., Lian, G., 2013b. Recent advances in predicting skin permeability of hydrophilic solutes. Advanced Drug Delivery Reviews 65, 295-305.

Choi, C.M., Berson, D.S., 2006. Cosmeceuticals, Seminars in Cutaneous Medicine and Surgery. Elsevier, pp. 163-168.

D'Amico, R.A., Saltz, R., Rohrich, R.J., Kinney, B., Haeck, P., Gold, A.H., Singer, R., Jewell, M.L., Eaves, F.I., 2008. Risks and opportunities for plastic surgeons in a widening cosmetic medicine market: Future demand, consumer preferences and trends in practitioners' services. Plastic and Reconstructive Surgery 121, 1787-1792.

Delmas, T., Piraux, H., Couffin, A.-C., Texier, I., Vinet, F., Poulin, P., Cates, M.E., Bibette, J., 2011. How to prepare and stabilise very small nanoemulsions. Langmuir 27, 1683-1692.

Denton, P., Rostron, C., 2013. Pharmaceutics: The Science of Medicine Design. Oxford University Press.

Dickinson, E., 2009. Hydrocolloids as emulsifiers and emulsion stabilisers. Food Hydrocolloids 23, 1473-1482.

Draelos, Z.D., 2014. Cosmeceuticals: Efficacy and Influence on Skin Tone. Dermatologic Clinics 32, 137-143.

Dykes, P., 1998. Surfactants and the skin. International Journal of Cosmetic Science 20, 53-61.

Eaglstein, W.H., 2014. What are cosmetics and cosmeceuticals?, The FDA for Doctors. Springer, pp. 29-31.

El Hussein, S., Muret, P., Berard, M., Makki, S., Humbert, P., 2007. Assessment of principal parabens used in cosmetics after their passage through human epidermis–dermis layers (*ex-vivo* study). Experimental Dermatology 16, 830-836.

Ema, M., Matsuda, A., Kobayashi, N., Naya, M., Nakanishi, J., 2012. Dermal and ocular irritation and skin sensitisation studies of fullerene C60 nanoparticles. Cutaneous and Ocular Toxicology 32, 128-134.

Forgiarini, A., Esquena, J., Gonzalez, C., Solans, C., 2001. Formation of nano-emulsions by low-energy emulsification methods at constant temperature. Langmuir 17, 2076-2083.

Freitas, F., Alves, V., Reis, M.M., 2014. Bacterial Polysaccharides: Production and Applications in Cosmetic Industry, in: Ramawat, K.G., Mérillon, J.-M. (Eds.), Polysaccharides. Springer International Publishing, pp. 1-24.

Fujimoto, T., Ito, S., Ito, M., Kanazawa, H., Yamaguchi, S., 2012. Induction of different reactive oxygen species in the skin during various laser therapies and their inhibition by fullerene. Lasers in Surgery and Medicine 44, 685-694.

Garcıa-Ochoa, F., Santos, V., Casas, J., Gomez, E., 2000. Xanthan gum: production, recovery, and properties. Biotechnology Advances 18, 549-579.

Garg, T., 2014. Current nanotechnological approaches for an effective delivery of bio-active drug molecules in the treatment of acne. Artificial Cells, Nanomedicine, and Biotechnology, 1-8.

GBI Research, 2013. Cosmeceuticals market to 2018–Technological advances and consumer awareness boost commercial potential for innovative and premium-priced products, http://www.researchandmarkets.com/reports/2393091/cosmeceuticals_market_to_2018_technological.

Gilbert, L., Picard, C., Savary, G., Grisel, M., 2013. Rheological and textural characterisation of cosmetic emulsions containing natural and synthetic polymers: relationships between both data. Colloids and Surfaces A: Physicochemical and Engineering Aspects 421, 150-163.

Golemanov, K., Tcholakova, S., Denkov, N.D., Gurkov, T., 2006. Selection of surfactants for stable paraffin-in-water dispersions, undergoing solid-liquid transition of the dispersed particles. Langmuir 22, 3560-3569.

Golubovic-Liakopoulos, N., Simonnet, J.-T., Sanford R, Shah, B., 2011. Nanotechnology Use with Cosmeceuticals, Seminars in Cutaneous Medicine and Surgery, pp. 176-180.

Griffin, W.C., 1949. Classification of surface-active agents by HLB. Journal of Society of Cosmetic Chemists 1, 311-326.

Griffin, W.C., 1954. Calculation of HLB values of non-ionic surfactants. Journal of Society of Cosmetic Chemists 5, 249-256.

Grigoriev, D.O., Miller, R., 2009. Mono- and multilayer covered drops as carriers. Current Opinion in Colloid & Interface Science 14, 48-59.

Gutiérrez, J., González, C., Maestro, A., Sole, I., Pey, C., Nolla, J., 2008. Nano-emulsions: New applications and optimisation of their preparation. Current Opinion in Colloid & Interface Science 13, 245-251.

Han, N.S., Basri, M., Abd. Rahman, M.B., Zaliha Raja Abd. Rahman, R.N., Salleh, A.B., Ismail, Z., 2011. Phase behavior and formulation of palm oil esters o/w nanoemulsions stabilised by hydrocolloid gums for cosmeceuticals application. Journal of Dispersion Science and Technology 32, 1428-1433.

Hoeller, S., Sperger, A., Valenta, C., 2009. Lecithin based nanoemulsions: a comparative study of the influence of non-ionic surfactants and the cationic phytosphingosine on physicochemical behaviour and skin permeation. International Journal of Pharmaceutics 370, 181-186.

Ikeda, A., Doi, Y., Hashizume, M., Kikuchi, J.-i., Konishi, T., 2007. An Extremely Effective DNA Photocleavage Utilising Functionalised Liposomes with a Fullerene-Enriched Lipid Bilayer. Journal of the American Chemical Society 129, 4140-4141.

Inui, S., Aoshima, H., Nishiyama, A., Itami, S., 2011. Improvement of acne vulgaris by topical fullerene application: unique impact on skin care. Nanomedicine: Nanotechnology, Biology and Medicine 7, 238-241.

Inui, S., Mori, A., Ito, M., Hyodo, S., Itami, S., 2014. Reduction of conspicuous facial pores by topical fullerene: possible role in the suppression of PGE2 production in the skin. Journal of Nanobiotechnology 12, 6.

Jarzycka, A., Lewińska, A., Gancarz, R., Wilk, K.A., 2013. Assessment of extracts of Helichrysum arenarium, Crataegus monogyna, Sambucus nigra in photoprotective UVA and UVB; photostability in cosmetic emulsions. Journal of Photochemistry and Photobiology B: Biology 128, 50-57.

Jiang, J., Mei, Z., Xu, J., Sun, D., 2013. Effect of inorganic electrolytes on the formation and the stability of water-in-oil (W/O) emulsions. Colloids and Surfaces A: Physicochemical and Engineering Aspects 429, 82-90.

Jiao, J., Burgess, D.J., 2003. Rheology and stability of water-in-oil-in-water multiple emulsions containing Span 83 and Tween 80. AAPS PharmSci 5, E7.

Kabri, T.-h., Arab-Tehrany, E., Belhaj, N., Linder, M., 2011. Physico-chemical characterisation of nano-emulsions in cosmetic matrix enriched on omega-3. Journal of Nanobiotechnology 9, 41.

Kamairudin, N., Gani, S.S., Masoumi, H.R., Hashim, P., 2014. Optimisation of natural lipstick formulation based on pitaya (*Hylocereus polyrhizus*) seed oil using D-optimal mixture experimental design. Molecules (Basel, Switzerland) 19, 16672-16683.

Kato, S., Kikuchi, R., Aoshima, H., Saitoh, Y., Miwa, N., 2010. Defensive effects of fullerene-C60/liposome complex against UVA-induced intracellular reactive oxygen species generation and cell death in human skin keratinocytes HaCaT, associated with intracellular uptake and extracellular excretion of fullerene-C60. Journal of Photochemistry and Photobiology B: Biology 98, 144-151.

Keng, P.S., Basri, M., Zakaria, M.R.S., Rahman, M.B.A., Ariff, A.B., Rahman, R.N.Z.A., Salleh, A.B., 2009. Newly synthesised palm esters for cosmetics industry. Industrial Crops and Products 29, 37-44.

Kennedy, P.E., 2015. Viruses, apoptosis, and neuroinflammation – a double-edged sword. Journal of Neurovirology 21, 1-7.

Kim, T., Kim, H., Cho, S., Kang, W., Baek, H., Jeon, H., Kim, B., Kim, D., 2011. *Nelumbo nucifera* extracts as whitening and anti-wrinkle cosmetic agent. Korean Journal of Chemical Engineering 28, 424-427.

Kligman, A., 2005. The Future of Cosmeceuticals: An Interview with Albert Kligman. Dermatologic Surgery 31, 890-891.

Kong, M., Chen, X.G., Kweon, D.K., Park, H.J., 2011. Investigations on skin permeation of hyaluronic acid based nanoemulsion as transdermal carrier. Carbohydrate Polymers 86, 837-843.

Kratschmer, W., Lamb, L.D., Fostiropoulos, K., Huffman, D.R., 1990. Solid C60: a new form of carbon. Nature 347, 354-358.

Krusic, P., Wasserman, E., Keizer, P., Morton, J., Preston, K., 1991. Radical reactions of C60. Science 254, 1183-1185.

Krutmann, J., Humbert, P., 2011. Nutrition for healthy skin. Springer.

Kubota, R., Tahara, M., Shimizu, K., Sugimoto, N., Hirose, A., Nishimura, T., 2011. Time-dependent variation in the biodistribution of C60 in rats determined by liquid chromatography–tandem mass spectrometry. Toxicology Letters 206, 172-177.

Lee, C.H., Singla, A., Lee, Y., 2001. Biomedical applications of collagen. International Journal of Pharmaceutics 221, 1-22.

Lee, M.-R., Lin, C.-Y., Li, Z.-G., Tsai, T.-F., 2006. Simultaneous analysis of antioxidants and preservatives in cosmetics by supercritical fluid extraction combined with liquid chromatography–mass spectrometry. Journal of Chromatography A 1120, 244-251.

Lens, M., 2009. Use of fullerenes in cosmetics. Recent Patents on Biotechnology 3, 118-123.

Liebl, M.P., Kaya, A.M., Tenzer, S., Mittenzwei, R., Koziollek-Drechsler, I., Schild, H., Moosmann, B., Behl, C., Clement, A.M., 2014. Dimerisation of visinin-like protein 1 is regulated by oxidative stress and calcium and is a pathological hallmark of amyotrophic lateral sclerosis. Free Radical Biology and Medicine 72, 41-54.

Lifshitz, I.M., Slyozov, V.V., 1961. The kinetics of precipitation from supersaturated solid solutions. Journal of Physics and Chemistry of Solids 19, 35-50.

Lintner, K., Mas-Chamberlin, C., Mondon, P., Peschard, O., Lamy, L., 2009. Cosmeceuticals and active ingredients. Clinics in Dermatology 27, 461-468.

López, A.M., Mateo-Alonso, A., Prato, M., 2011. Materials chemistry of fullerene C 60 derivatives. Journal of Materials Chemistry 21, 1305-1318.

Lovelyn, C., Attama, A.A., 2011. Current State of Nanoemulsions in Drug Delivery. Journal of Biomaterials & Nanobiotechnology 2.

Lynde, C., 2001. Moisturisers: what they are and how they work. Skin Therapy Letter 6, 3-5.

MacNeil, S., 2007. Progress and opportunities for tissue-engineered skin. Nature 445, 874-880.

Madison, K.C., 2003. Barrier function of the skin:“la raison d'etre” of the epidermis. Journal of Investigative Dermatology 121, 231-241.

Magari, R.T., Munoz-Antoni, I., Baker, J., Flagler, D.J., 2004. Determining shelf life by comparing degradations at elevated temperatures. Journal of Clinical Laboratory Analysis 18, 159-164.

Masaki, H., 2014. Antioxidants and Skin Aging, Systems Biology of Free Radicals and Antioxidants. Springer, pp. 3785-3801.

McClements, D.J., 2012. Nanoemulsions versus microemulsions: terminology, differences, and similarities. Soft Matter 8, 1719-1729.

Mendes, A.C., Baran, E.T., Pereira, R.C., Azevedo, H.S., Reis, R.L., 2012. Encapsulation and survival of a chondrocyte cell line within xanthan gum derivative. Macromolecular Bioscience 12, 350-359.

Menon, G.K., Cleary, G.W., Lane, M.E., 2012. The structure and function of the stratum corneum. International Journal of Pharmaceutics 435, 3-9.

Mitra, R.K., Paul, B.K., 2005. Physicochemical investigations of microemulsification of eucalyptus oil and water using mixed surfactants (AOT+Brij 35) and butanol. Journal of Colloid and Interface Science 283, 565-577.

Musa, S.H., Basri, M., Masoumi, H.R.F., Karjiban, R.A., Malek, E.A., Basri, H., Shamsuddin, A.F., 2013. Formulation optimisation of palm kernel oil esters nanoemulsion-loaded with chloramphenicol suitable for meningitis treatment. Colloids and Surfaces B: Biointerfaces 112, 113-119.

Nakazawa, H., Ohta, N., Hatta, I., 2012. A possible regulation mechanism of water content in human stratum corneum via intercellular lipid matrix. Chemistry and Physics of Lipids 165, 238-243.

Nanjwade, B.K., Kadam, V.T., Srichana, T., 2013. Nanoemulsions Formation and Their Potential Applications. Reviews in Nanoscience and Nanotechnology 2, 261-274.

Naylor, E.C., Watson, R.E.B., Sherratt, M.J., 2011. Molecular aspects of skin ageing. Maturitas 69, 249-256.

Nikolić, N., Vranješ-Đurić, S., Janković, D., Đokić, D., Mirković, M., Bibić, N., Trajković, V., 2009. Preparation and biodistribution of radiolabeled fullerene C60 nanocrystals. Nanotechnology 20, 385102.

Nosik, D.N., Lialina, I.K., Kalnina, L.B., Lobach, O.A., Chataeva, M.S., Rasnetsov, L.D., 2009. The anti-retroviral agent Fullevir. Voprosy Virusologii 54, 41-43.

Palaniraj, A., Jayaraman, V., 2011. Production, recovery and applications of xanthan gum by Xanthomonas campestris. Journal of Food Engineering 106, 1-12.

Pardeike, J., Hommoss, A., Müller, R.H., 2009. Lipid nanoparticles (SLN, NLC) in cosmetic and pharmaceutical dermal products. International Journal of Pharmaceutics 366, 170-184.

Pathan, I.B., Setty, C.M., 2011. Enhancement of transdermal delivery of tamoxifen citrate using nanoemulsion vehicle. International Journal PharmTech Research 3, 287-297.

Patravale, V.B., Mandawgade, S.D., 2008. Novel cosmetic delivery systems: an application update. International Journal of Cosmetic Science 30, 19-33.

Paul, S., Panda, A., 2011. Physico-Chemical Studies on Microemulsion: Effect of Cosurfactant Chain Length on the Phase Behavior, Formation Dynamics, Structural Parameters and Viscosity of Water/(Polysorbate-20 + n-Alkanol)/n-Heptane Water-in-Oil Microemulsion. Journal Surfactants and Detergents 14, 473-486.

Peng, C., Yan, X., Tang, X., 2010. Preparation and characterisation of a triamcinolone acetonide palmitate submicron emulsion. Asian Journal of Pharmaceutical Sciences 5, 61-73.

Pouillot, A., Polla, A., 2013. Penetration of Cosmetics Into and Through the Stratum Corneum. Cosmetics & Toiletries.

Pouton, C.W., 2006. Formulation of poorly water-soluble drugs for oral administration: Physicochemical and physiological issues and the lipid formulation classification system. European Journal of Pharmaceutical Sciences 29, 278-287.

Pouton, C.W., Porter, C.J.H., 2008. Formulation of lipid-based delivery systems for oral administration: Materials, methods and strategies. Advanced Drug Delivery Reviews 60, 625-637.

Proksch, E., Brandner, J.M., Jensen, J.M., 2008. The skin: an indispensable barrier. Experimental Dermatology 17, 1063-1072.

Puglia, C., Bonina, F., 2012. Lipid nanoparticles as novel delivery systems for cosmetics and dermal pharmaceuticals. Expert Opinion on Drug Delivery 9, 429-441.

Rahn-Chique, K., Puertas, A.M., Romero-Cano, M.S., Rojas, C., Urbina-Villalba, G., 2012. Nanoemulsion stability: Experimental evaluation of the flocculation rate from turbidity measurements. Advances in Colloid and Interface Science 178, 1-20.

Raoof, M., Mackeyev, Y., Cheney, M.A., Wilson, L.J., Curley, S.A., 2012. Internalisation of C60 fullerenes into cancer cells with accumulation in the nucleus via the nuclear pore complex. Biomaterials 33, 2952-2960.

Rawlings, A.V., Canestrari, D.A., Dobkowski, B., 2004. Moisturiser technology versus clinical performance. Dermatologic Therapy 17, 49-56.

Rawlings, A.V., Harding, C.R., 2004. Moisturisation and skin barrier function. Dermatologic Therapy 17, 43-48.

Rebolleda, S., Sanz, M.T., Benito, J.M., Beltrán, S., Escudero, I., González San-José, M.L., 2015. Formulation and characterisation of wheat bran oil-in-water nanoemulsions. Food Chemistry 167, 16-23.

Rezaee, M., Basri, M., Rahman, R.N.Z.R.A., Salleh, A.B., Chaibakhsh, N., Karjiban, R.A., 2014. Formulation development and optimisation of palm kernel oil esters-based nanoemulsions containing sodium diclofenac. International Journal of Nanomedicine 9, 539.

Sadoqi, M., Lau-Cam, C.A., Wu, S.H., 2009. Investigation of the micellar properties of the tocopheryl polyethylene glycol succinate surfactants TPGS 400 and TPGS 1000 by steady state fluorometry. Journal of Colloid and Interface Science 333, 585-589.

Salim, N., Basri, M., Rahman, M.B., Abdullah, D.K., Basri, H., 2012. Modification of palm kernel oil esters nanoemulsions with hydrocolloid gum for enhanced topical delivery of ibuprofen. International Journal of Nanomedicine 7, 4739.

Shinohara, N., Matsumoto, K., Endoh, S., Maru, J., Nakanishi, J., 2009. In vitro and in vivo genotoxicity tests on fullerene C60 nanoparticles. Toxicology Letters 191, 289-296.

Solè, I., Solans, C., 2013. Nanoemulsions. Encyclopedia of Colloid and Interface Science, 733-747.

Soni, M.G., Carabin, I.G., Burdock, G.A., 2005. Safety assessment of esters of p-hydroxybenzoic acid (parabens). Food and Chemical Toxicology 43, 985-1015.

Sonneville-Aubrun, O., Simonnet, J.-T., L'alloret, F., 2004. Nanoemulsions: a new vehicle for skincare products. Advances in Colloid and Interface Science 108, 145-149.

Tadros, T., Izquierdo, P., Esquena, J., Solans, C., 2004. Formation and stability of nano-emulsions. Advances in Colloid and Interface Science 108–109, 303-318.

Tadros, T.F., 2013. Use of Rheological Measurements for Assessment and Prediction of the Long-Term Assessment of Creaming. Product Design and Engineering: Formulation of Gels and Pastes.

Takada, H., Mimura, H., Xiao, L., Islam, R., Matsubayashi, K., Ito, S., Miwa, N., 2006. Innovative Anti-Oxidant: Fullerene as “Radical Sponge” on the Skin. Its High Level of Safety, Stability and Potential as Premier Anti-Aging and Whitening Cosmetic Ingredient. Fullerenes, Nanotubes, and Carbon Nanostructures 14, 335-341.

Tal-Figiel, B., Figiel, W., 2008. Micro- and Nanoemulsions in Cosmetic and Pharmaceutical Products. Journal of Dispersion Science and Technology 29, 611-616.

Talegaonkar, S., Negi, L., 2015. Nanoemulsion in Drug Targeting, in: Devarajan, P.V., Jain, S. (Eds.), Targeted Drug Delivery: Concepts and Design. Springer International Publishing, pp. 433-459.

Thakur, N., Garg, G., Sharma, P., Kumar, N., 2012. Nanoemulsions: A Review on Various Pharmaceutical Application. Global Journal of Pharmacology 6, 222-225.

Tzirakis, M.D., Orfanopoulos, M., 2013. Radical Reactions of Fullerenes: From Synthetic Organic Chemistry to Materials Science and Biology. Chemical Reviews 113, 5262-5321.

Tzoupis, H., Leonis, G., Durdagi, S., Mouchlis, V., Mavromoustakos, T., Papadopoulos, M., 2011. Binding of novel fullerene inhibitors to HIV-1 protease: insight through molecular dynamics and molecular mechanics Poisson–Boltzmann surface area calculations. Journal of Computer-Aided Molecular Design 25, 959-976.

Viyoch, J., Klinthong, N., Siripaisal, W., 2003. Development of Oil-in-Water Emulsion Containing Tamarind Fruit Pulp Extract I. Physical Characteristics and Stability of Emulsion. Naresuan University Journal 11, 29-44.

Wagner, C., 1961. Theorie der Alterung von Niederschlägen durch Umlösen (Ostwald-Reifung). Zeitschrift für Elektrochemie, Berichte der Bunsengesellschaft für physikalische Chemie 65, 581-591.

Waller, J.M., Maibach, H.I., 2006. Age and skin structure and function, a quantitative approach (II): protein, glycosaminoglycan, water, and lipid content and structure. Skin Research and Technology 12, 145-154.

Wang, I.C., Tai, L.A., Lee, D.D., Kanakamma, P., Shen, C.K.-F., Luh, T.-Y., Cheng, C.H., Hwang, K.C., 1999. C60 and water-soluble fullerene derivatives as antioxidants against radical-initiated lipid peroxidation. Journal of Medicinal Chemistry 42, 4614-4620.

Xiao, L., Matsubayashi, K., Miwa, N., 2007. Inhibitory effect of the water-soluble polymer-wrapped derivative of fullerene on UVA-induced melanogenesis via downregulation of tyrosinase expression in human melanocytes and skin tissues. Archives of Dermatological Research 299, 245-257.

Yaghmur, A., De Campo, L., Aserin, A., Garti, N., Glatter, O., 2004. Structural characterisation of five-component food grade oil-in-water nonionic microemulsions. Physical Chemistry Chemical Physics 6, 1524-1533.

Zeeb, B., Gibis, M., Fischer, L., Weiss, J., 2012. Influence of interfacial properties on Ostwald ripening in crosslinked multilayered oil-in-water emulsions. Journal of Colloid and Interface Science 387, 65-73.

Zhang, X.-J., Chinkes, D.L., Wolfe, R.R., 2003. Measurement of protein metabolism in epidermis and dermis. American Journal of Physiology-Endocrinology and Metabolism 284, E1191-E1201.

Zhou, C., Liu, Q., Xu, W., Wang, C., Fang, X., 2011. A water-soluble C 60-porphyrin compound for highly efficient DNA photocleavage. Chemical Communications 47, 2982-2984.

Zinoviadou, K.G., Scholten, E., Moschakis, T., Biliaderis, C.G., 2012. Engineering interfacial properties by anionic surfactant–chitosan complexes to improve stability of oil-in-water emulsions. Food & Function 3, 312-319.