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The International Conference on Pharmacy and Advanced Pharmaceutical Sciences

Faculty of Pharmacy UGM

PROCEEDING

The International Conference on Pharmacy and Advanced Pharmaceutical Sciences

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Yogyakarta Indonesia
October 2009

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Preface from the Editor

The proceeding was produced based on papers and posters presented at the international Conference on Pharmacy and Advanced Pharmaceutical Sciences, held in Yogyakarta, Indonesia, 5 – 6 October 2009.

The proceeding clearly reflects broad interest; from there are participants coming from all around the world. Many contributions on Pharmaceutical Sciences there are quite a substantial number of papers on Pharmacist role in general. The papers presented file into a broad spectrum in Pharmaceutical sciences including Pharmacology, Toxicology, Analytical Chemistry and Drug Design, Drugs Synthesis, Formulation of Drugs, Pharmacy Social, Pharmacoepidemy, Traditional Medicine Natural Product Chemistry and Phytochemistry, etc.

In addition there are substantial numbers of paper deal with professional aspect of Pharmacist in general health care.

In this an opportunity, I would like to express my appreciation to the editorial team of the proceeding who have been working hard to review manuscripts, and making the first edition of this proceeding be possible.

I would like also to thanks to all invited speakers and presenters who participated in the International Conference on Pharmacy and Advanced Pharmaceutical Sciences and your contribution to this proceeding.

Finally, I hope this proceeding will give contribution to the advanced scientific research in the field of pharmaceutical sciences

Yogyakarta, July 2010

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Welcome Message
From the committee

Welcome to Yogyakarta

On behalf of the Scientific and Organizing Committees, it is a great pleasure for me to welcome all participants to Yogyakarta, to the International Conference on Pharmacy and Advanced Pharmaceutical Science 2009.
The international conference is organized by the faculty of Pharmacy UGM to celebrate its 63th anniversary and the Lustrum XII of Gadjah Mada University, as a collaboration work between the Faculty of Pharmacy UGM with the Nara Institute of Science and Technology (Japan) and the Universiti Sains Malaysia (Malaysia). In this conference 15 lectures within the field of Pharmaceutical Care and Advanced Pharmaceutical Science will be given by invited speakers. Besides, 55 posters and 75 paper will be presented in the parallels presentation sessions. Herewith, we express our gratitude to all speakers and presenter, who would like to share their advance knowledge in this scientific event.

The Organizing Committee gratefully acknowledges the Nara Institute of Science and Technology and the Universiti Sains Malyasia, for the nice collaboration in bringing forth this conference. A special acknowledgment is addressed to the Rector of Gadjah Mada University and the sponsors, for all supports that make this symposium possible. Furthermore, personally, I want to express my deep appreciation to the members of the Organizing Committee, for the good teamwork and their great effort given in the preparation for this symposium.

Finally, I wish all participants a scientifically rewarding and an enjoyable meeting in Yogyakarta.

Chairman

Dr. Hilda Ismail, M.Si., Apt.

Remark of the Dean Faculty

Assalamu'alaikum wr. wb.
Distinguished ladies & gentlemen.

First of all, on be half of the Faculty of Pharmacy Universitas Gadjah Mada, I would like come to all of you in Yogyakarta, thank you very much for your attention to come and to attend the international Symposium on Pharmacy and Advanced Pharmaceutical Sciences. I hope we are all in health condition.

Ladies and gentlemen,
The symposium is organized by the Faculty of Pharmacy UGM in collaboration with the Faculty of Pharmaceutical Sciences Universiti Sains Malaysia and the Nara Institute of Science and Technology Japan, and held as part to celebrate the 63th anniversary of the Faculty of Pharmacy UGM.
In the symposium , I hope we can communicate our recently information concerning social / clinical pharmacy and pharmaceutical sciences. I hope the symposium will be very fruitfull, very useful for all of us .
I addres special thanks to the plenary speakers both from domestic and aboard, the oral and poster presenters, as well as to those who come just to know the development of clinical or social pharmacy and pharmaceutical science. Your willingness to come , to communicate and to share your experiences is highly appreciated.

Special thanks also I address to my colleague the Dean of Faculty of Pharmacy USM who has been coordinating USM students to attend this symposium. The hope is not to set up networking between the pharmacy students of USM and UGM.

Therefore, during almost whole day discussing scientific matter related to human health and welfare, I hope we can make a wonderful opportunity to make a scientific closer relationship while we enjoy the cultural performances of Yogyakarta presented by our pharmacy student.

Finally, I hope that this meeting will give benefits to all of us, and we may see each other again in a similar event in the near future.

I look forward to thank you all for attending this event.

Wassalamu'alaikum wa rahmatullahi wa barakatuh,
Dean of Faculty of Pharmacy UGM

Prof. Dr. Marchaban, DESS., Apt.

Speech of the Senior Vice Rector
For Education, Research and Community Services,
Gadjah Mada University

Assalamu'alaikum wa rahmatulLahi wa barakatuh,

On behalf of the Rector, I would like to welcome all of you to our campus Gadjah Mada University and to our home town Yogyakarta. It is a great honor for me and Gadjah Mada University to host the Two-day International Conference on Pharmacy and Pharmaceutical Sciences that is conducted by the Faculty of Pharmacy, Gadjah Mada University. The increasing problems and new cases of some diseases in the world, both the infectious and the degenerative diseases, have demanded the development of medical and pharmaceutical sciences and technologies for supporting the developments of early detection methods of the diseases, the accurate diagnoses, as well as the appropriate and effective medications or therapy. Pharmaceutical Science and Technology have been developing very fast within recent years. The development trend shows using much more biotechnological approach in both diagnose establishment and medication administrations. For examples the usage of some serums, enzymes, hormones, vaccines, etc., and their recombinant products. The science and technology for finding prevention method against infectious diseases or degenerative diseases now have been developing so amazing, for example the usage of growth hormones, vaccines, and stem cells for it.

Gadjah Mada University has been committed to become World Class University; therefore international networking in education, research and publication is much needed. I really support to this international conference on Pharmaceutical Science and Technology which can keep us in touch with the state of the art of pharmaceutical science. I do believe that by conducting this kind of international meeting, we can get and exchange new information and best practices on pharmaceutical science and technology, and it is very important to inspire our young researchers and enhance our research networking internationally. In this occasion, I would like to express my great gratitude to all the guest speakers and speakers, who have contributed their advanced presentations in this international conference. I also would like to extend my gratitude to the Organizing Committee from the Faculty of Pharmacy, Gadjah Mada University, who has already successfully arranged this international conference. I would also thank to all institutions or companies who have sponsored and supported this conference.

Finally, have a fruitful conference and enjoy Yogyakarta. Thank you
Wassalamu'alaikum wa rahmatulLahi wa barakatuh,

Senior Vice Rector for Education, Research and Community Service
Gadjah Mada University

Prof. Dr. Retno Sunarminingsih, M.Sc., Apt.

CONTENTS

The Influence of Arbutin and Olive Oil as an Enhancer in Characteristic and SPF Value of Sunscreen (Combination of Oxybenzone and Octyldimethyl Paba in *Carbomer* 940 Gel Base)

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Abstract

The aim of this research was to understand the influence of arbutin (3% w/w) and olive oil addition and the increase of olive oil concentration (3, 5, and 7% w/w) on characteristic and SPF value of sunscreen product containing oxybenzone and octyldimethyl PABA (3 : 7% w/w) in a *carbomer* 940 gel base. The characteristic test was done by observing the physical appearance, pH and spreading ability on the 2nd day after the product was made; while the measuring of SPF value was done with a spectrophotometric method. The result of the characteristic test showed that the addition of arbutin and olive oil affect the physical appearance (organoleptic and consistency) of sunscreen product as well as its spreading ability but has no effect on pH; while the significant raise in SPF value of the sunscreen formula showed that the addition of arbutin and olive oil affect the effectiveness of sunscreen product and an increase in olive oil concentration has lead to an increase in SPF value. Considering the result of this research, it's suggested to perform a further research to comprehend the in vivo effectiveness of this product on human skin.

Key words: Arbutin, Olive oil, Oxybenzone, Octyldimethyl PABA, Sun Protection Factor

Introduction

Exposure to sunlight can have both advantageous and harmful effects on the human body. Adverse reaction to the UV sun rays includes erythema, tanning, sunburn, photo ageing, hyper pigmentation, photosensitivity and skin cancers [Tranggono and Latifah, 2007; Wilkinson *et al*, 1973]. Protecting for the skin from harmful effects of solar radiation can be done by using sunscreens. Active ingredients in sunscreens are divided to physical and chemical agents. Physical sunscreen agents reflect the UV rays from the skin. They are not transparant and accordingly need high concentration to be effective, which made them not preferable for some people. Chemical sunscreen agents absorbing UV-A radiation i.e. (oxybenzone) and absorbing UV-B radiation such as i.e. (octyldimethyl PABA). To obtain a higher protection effect with broad spectrum sunscreen, a combination of an anti UV-A and anti UV-B sunscreen agents are recently been used in many sunscreen product [Widianingsih and Lumintang, 2002].

Normally, skin has its own protection mechanism against the harmful effect of UV rays, such as thickening of *stratum corneum*, sweating, and skin pigmentation. The abnormal increase of melanin as a result of skins natural protection can result in a non homogenous skin color, which is usually disliked by a lot of people. To solve this problem, whitening agents are used to control the production and metabolism of melanin in epidermis. One example of a frequently used whitening agent is arbutin, a hydroquinone derivates which inhibits melanin production. Arbutin has lower toxicity than hydroquinone's and its depigmentation effect is higher than kojic acid and vitamin C [Mashhood, 2006]. This substance is used as whitening agent at various concentration, in the range of 0.5-3.0%. It has a low partition coefficient and penetration rate, which accordingly needs addition of a penetration enhancer to make it work optimally [Zulkarnain, 2003; Galilee, 2008; Mitsui, 1998].

Olive oil is a pure oil obtained from *Olea europaea* Linn containing oleic acid (83.5%), a substance that is capable to interact and modify the lipid bilayer of stratum corneum, in order to increase the lipofilicity of a substance. Its ability as penetration enhancer in local anesthetic agent has been proofed by Sarma and Fisher [Sarma, 1993]. Olive oil has been widely used in sunscreen and other cosmeceutical preparation for its emollient activity, it is

nonirritant and considered as a natural lipid that has the highest compatibility with human skin [Rowe *et al*, 2003; O'Neil, 2006].

There is a wide variety of sunscreen preparations that available in the market such as cream, lotion and gel. Among these, gels gives cool sensation, not sticky, elegant, smooth and easy to be removed by washing. A synthetic gelling agent usually just required in a small amount to produce a gel with good consistency. Regarding this *carbomer* 940 as the synthetic geiling agent is considered to be the most suitable for this study.

In this study a combination of oxybenzone 3% w/w (anti UV-A) and octyldimethyl PABA 7% w/w (anti UV-B) [Pratiwi, 2006] together with arbutin 3% w/w and various concentration of olive oil (3, 5, and 7% w/w) in a *carbomer* 940 gel base are used in the formula, then the change in SPF value are observed by spectrophotometric method.

Methodology

Materials

Materials used in the experiment were Oxybenzone (Surya Dermato), Octyldimethyl PABA (Surya Dermato), Arbutin (Asia Visions Ltd.), Olive oil (Brataco Chemicals), *Carbomer* 940 (Brataco Chemicals), Triethanolamine (Surya Dermato), EDTA Sodium (Surya Dermato), Methyl paraben (Surya Dermato), Propyl paraben (Surya Dermato), BHT (Brataco Chemicals), *Tween* 80 (Surya Dermato), Propylene glycol (Brataco Chemicals), Isopropanol *p.a.* (Brataco Chemicals). All ingredients used having pharmaceutical grade except isopropanol which was in pro analytical grade.

The qualitative analysis is carried out in a *Fourier Transform Infrared Spectrophotometre* Jasco FT-IR 5300, *Melting Point Apparatus*, *Bausch and Lomb Refractometre*. The results were compared to the reference and substance certificate of analysis.The SPF assay were carried out by using a *Double Beam* UV-Vis *Spectrophoto-meter* Perkin Elmer Lambda EZ 201, *Ultrasonic Branson* 3510, *Hettich zentrifugen* EBA 20, Mettler Toledo AL 204 analytical balance. Digital pH meter Schott CG 842 and spreading-capacity measurer are also used for the organoleptic analysis.

Table 1: Formula used in experiment

Composition	Function	Concentration in formula (% w/w)				
		S	S+A	S+A+O 3%	S+A+O 5%	S+A+O 7%
Oxybenzone	Sunscreen agent	3	3	3	3	3
Octyldimethyl PABA	Sunscreen agent	7	7	7	7	7
Arbutin	Whitening agent	0	3	3	3	3
Tween 80	Emulgator	0.5	0.5	0.5	0.5	0.5
Olive oil	Enhancer	0	0	3	5	7
Carbomer	Geling agent	1	1	1	1	1
Distilled water up to	Solvent	100	100	100	100	100

* S = Sunscreen
S+A = Sunscreen + Arbutin
S+A+O 3% = Sunscreen + Arbutin + Olive oil 3%
S+A+O 5% = Sunscreen + Arbutin + Olive oil 5%
S+A+O 7% = Sunscreen + Arbutin + Olive oil 7%

Preparation of sunscreen gel containing arbutin and olive oil

EDTA Sodium was first dissolved in distilled water, then an amount of *carbomer* was dispersed in it. This dispersion then was left for a night after the pH was adjusted to 6 with addition of Tri Ethanol Ammine (TEA). Methyl-paraben and Propyl-paraben were dissolved in propylene glycol and then poured into the mixture of *carbomer* and stirred to create a good gel base.

Arbutin was dissolved in distilled water then Tween 80 was added. The solution of BHT in olive oil was mixed together in it to form a good emulsion system. Oxybenzone, Octyldimethyl PABA and propylene glycol were mixed and put into the emulsion system and stirred well before inserted into the gel base and stirred well to form the sunscreen gel. The sunscreen were then kept in a tight container and stored well for further analysis. Other treatment formulas were similarly made with main composition as in Table 1.

Characteristics determination of sunscreens gel

Organoleptic test are done visually after preparation, while determination of pH and spreading-capacity are done 2 days after the formula done. By using a Digital pH meter Schott CG 842, and a spreading-capacity measurer.

To determine the pH, 2 grams of the sunscreen gels was mixed thoroughly with 18 ml of water free-CO_2 then the pH wasmeasured with pH meter.

To determine the spreading-capacity, approximately 1 gram of the gels are placed on a glass plate with a millimeter scale. This glass plate is then covered with another glass plate, then the change in gell-spreading is observed along with an increase of the given load.

Determination of SPF value of sunscreens gel

To observe the effect on SPF caused by arbutin and olive oil addition, 100.0 mg sunscreens dissolved in 2.0 ml isopropanol, then solution are centrifuged for 15 minutes at 50 rpm speed. 1.0 ml of the filtrate is taken and poured into a 5.0 ml metered flask and shake well until its homogenized (10000 ppm).

The 1.0 ml mixture was then pipette, and put into a 10.0 ml metered flask than diluted to acquire a 1000 ppm solution. The 1000 ppm solution that are acquired was pipette for 1.0 ml solution and moved into another 10.0 ml metered flask before isopropanol was added to dilute it and then shacked well to reach a concentration of 100 ppm (contains 10 ppm sunscreen's active ingredients). UV spectrum of this solution was measured at 290-400 nm by using *Double Beam* UV-Vis *Spectrophotometer* Perkin Elmer Lambda EZ 201 at interval of 2 nm, which has an absorption that is larger than 0.050.

According to the method used by Petro, the absorption data received were converted into the absorption value on 10 ppm concentration for each wavelength. The AUC of each formula from the shortest and longest wavelength are counted using the following equation:

$$AUC_{\lambda_{p-\alpha}}^{\lambda_p} = \frac{A_{p-\alpha} + A_p}{2} \lambda_p - \lambda_{p-\alpha}$$

Whereas:
AUC = Area under Curve
Ap = Absorbtion on p wavelength
Ap-α = Absorbtion on p-α wavelength

A total of AUC were obtained by adding each AUC between 2 wavelengths in series from 290 nm till 400 nm which has an absorption value above 0.050 and the SPF value of a formula were obtained by inserting the total AUC into the equation below:

$$Log\ SPF = \frac{Total\ area}{\lambda n - \lambda 1}\ x\ 2$$

Whereas:
λn= longest wavelength above 290 nm that has an absorption value higher than 0.050
λ1= shortest wavelength 290 nm

The Log SPF value is obtained from the equation was then converted into SPF value.

Statistical analysis

The coefficients variation of all data obtained from the experiment were calculated to ensure the homogeneity of the formula. One-way ANOVA were used to assess the significant of differences. In case of F significant value, multiple comparison Tukey test was used to compare the means of different treatment groups. Result $p<0.05$ were considered to be statistically significant.

Results and Discussions

The average data of organoleptic observation from all the sunscreen formula were shown in Table 2. His shown that they are different before and after addition of olive oil to the formula. What determines the color and smell of the sunscreen was the active ingredients olive oil is added to the formula, an ascend in the viscosity of formula was observed as a result of an increase in the amount of olive oil added. The addition of olive oil also influence the color and smell of sunscreen as it becomes stronger and more likely to take after the color and smell of the olive oil along with an increase in olive oil concentration.

Table 2: Organoleptic analysis of the sunscreens formula

Formula	Colour	Smell	Consistency
Gel base	Transparent	Octyldimethyl PABA	A bit viscous
Sunscreen (S)	Yellowish white	Octyldimethyl PABA	Not very viscous
S+Arbutin (A)	Yellowish white	Octyldimethyl PABA	Viscous
S+A+Olive oil (O) 3%	Yellowish	Olive oil	Viscous
S+A+O 5%	Yellowish	Olive oil	Very viscous
S+A+O 7%	Yellowish	Olive oil	Very viscous

Table 3: Average pH data

Formula	pH (average)	% var. coefficient
Gel base	6.60 ± 0.08	1.29
Sunscreen (S)	6.27 ± 0.05	0.79
S+Arbutin (A)	6.31 ± 0.05	0.74
S+A+Olive oil (O) 3%	6.31 ± 0.03	0.43
S+A+O 5%	6.30 ± 0.05	0.86
S+A+O 7%	6.29 ± 0.02	0.37

* The result were obtained from an average of 3 times replication

Table 4: Result of HSD test of the sunscreens pH

Formula	N	pH Classification α=0.05	
		1	2
S	9	6.27	
S+A+O 7%	9	6.29	
S+A+O 5%	9	6.30	
S+A	9	6.31	
S+A+O 3%	9	6.31	
Gel base	3		6.60

Table 5: Average slope of sunscreens formula

Formula	Average slope	% Var. coefficient
Gel base	0.2833 ± 0.0057	-
Sunscreen (S)	0.3359 ± 0.0076	2.26
S+Arbutin (A)	0.3859 ± 0.0119	3.09
S+A+Olive oil (O) 3%	0.2713 ± 0.0094	3.47
S+A+O 5%	0.2474 ± 0.0072	2.91
S+A+O 7%	0.2238 ± 0.0028	1.25

* The result were obtained from an average of 3 times replication

One of the important factors that influence sunscreen SPF value is the pH beside extinction coefficient and solvent polarity. Therefore, it's important to make sure reaction caused the SPF changes in the treatment formula. The pH of sunscreen

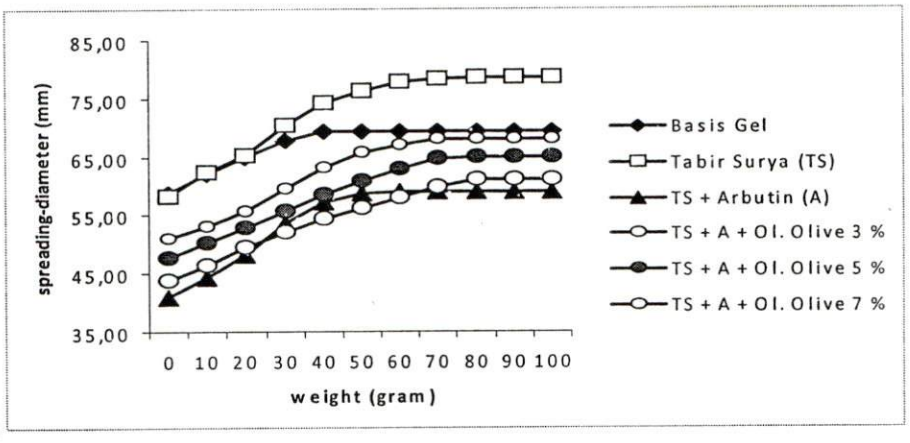

Figure 1: Spreading capability of sunscreen

gels also play a major rule in the sunscreen gels characteristic as the *carbomer* consistency were heavily affected by its acidity, a high acidity condition would lower the gels viscosity.

The result of pH analysis has shown that no significant difference whether there was addition of arbutin or olive oil as well as increase in olive oil concentration. From the data we see that the sunscreen formula were all in a range of skin pH (Tab 3. and Tab 4). The spreading capabilities of the formula were measured and the results were shown in table 5: From the data we could see that the spreading-capacity of the formula decline with the addition of arbutin and with a rise in olive oil concentration as a result of an increase in its viscosity.

The SPF analyses were done by extracting the sunscreen from its base with isopropanol. In order to assure that the base gel *carbomer* 940 will not give any absorbtion in the UV spectrum, it was extracted using isopropanol and observed at the wavelength of 290-400 nm. From the spectra it's known that the gel base did not give any absorbtion, therefore it's assumed that any change within the observation of SPF value were caused by the active ingredient only. To ensure the homogeneity in the formula, the % variation

coefficient of each sampling in each replication and % variation coefficient of each replication of each formula were calculated. The SPF value that resulted from the calculation (Tab 6.) was then compared to the American Society of Health System Pharmacist standard in order to know its protection capability.

This standard contains two different category of protection against UV rays as presented in Table 7.

Table 6: SPF data from the treatment formula

Formula	Replication	SPF (average)*	% var. coefficient *	SPF (average)**	% var. coefficient **
Sunscreen (S)	1	6.73	2.08	6.66	4.09
	2	6.56	2.36		
	3	6.68	1.71		
S+Arbutin (A)	1	9.20	1.98	9.09	2.79
	2	9.11	4.20		
	3	8.97	2.23		
S+A+Olive oil (O) 3%	1	11.91	3.63	12.02	3.14
	2	11.84	1.73		
	3	12.30	3.27		
S+A+O 5%	1	19.74	2.85	19.53	2.53
	2	19.44	3.29		
	3	19.41	1.96		
S+A+O 7%	1	26.30	2.18	25.92	3.44
	2	25.21	3.08		
	3	26.25	4.55		

*The data were obtained from 3 different samples in 1 product
**The data were obtained from an average of 3 different products in 1 formula

Table 7: Sunscreens category based on SPF value

Category	SPF	Protection	
		sunburn	tanning
Minimum	2-<4	Minimum	-
Moderate	4-<8	Moderate	Small
High	8-<12	High	Limited
Very high	12-<20	Very high	Large
Ultra	20-30	Maximum	Maximum

*American Health System Pharmacist, 2002

Table 8: The sunscreen's formula protection category

Formula	SPF (average)	Protection category
Sunscreen (S)	6.66	Moderate
S+Arbutin (A)	9.09	High
S+A+Olive oil (O) 3%	12.02	Very high
S+A+O 5%	19.53	Very high
S+A+O 7%	25.92	Maximum

From the data that were shown in Table 6, it can conclude that all of the sunscreen formulas during the experiment were homogeny and reproducible because its variation coefficient were less than 6%. These results were also supported from the amount of variation coefficient that was acquired from the pH value and the spreading-capability assessment that were also less than 6%.

According to the comparisons that were made above, the sunscreen's formula were ctegorized as given in Table 8. The result of HSD test presented in Table 9 indicate that there

was an increase in the SPF value of the sunscreen gels from moderate to maximum protection together with the addition of arbutin and an increase in olive oil concentration in the formula.

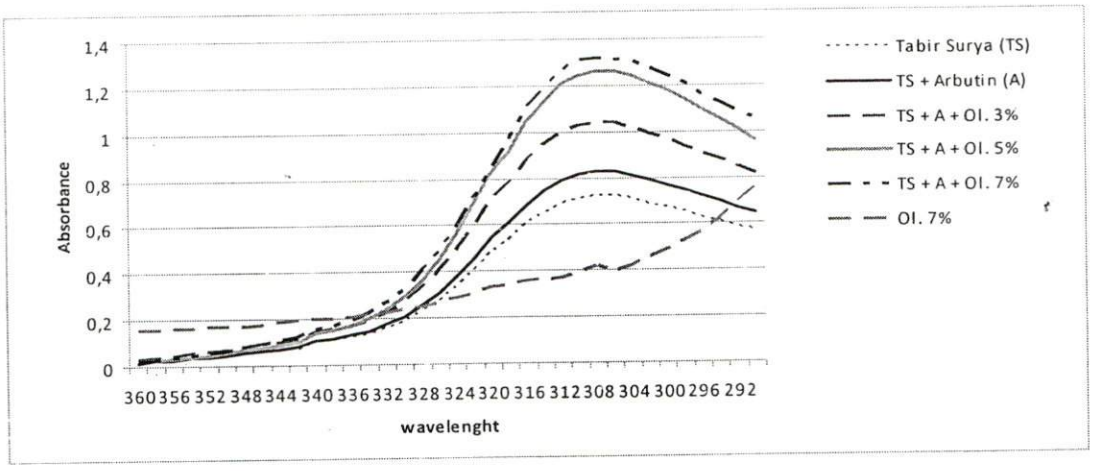

Figure 2: Absorbtion spectrum of sunscreen.

Table 9: Result of HSD test of the sunscreens SPF

Formula	N	SPF category α=0.05				
		1	2	3	4	5
Sunscreen (S)	9	6.60				
S+Arbutin (A)	9		9.09			
S+A+Olive oil (O) 3%	9			12.02		
S+A+O 5%	9				19.53	
S+A+O 7%	9					25.99

The table 9 shown that the addition of arbutin and olive oil has significantly elevated the SPF value of sunscreen gels and the maximum protection was given by the formula that contains 7% concentration of olive oil.

From the screening above (Fig 2.), it has been studied that the addition of arbutin and olive oil did not cause any movement on the maximum wavelength. Nevertheless, an increase in the intensity of absorbtion was observed. Thus it's predicted that an interaction occurred between the molecule of arbutin and sunscreen agent which intensify the effect of aucsochrome group and a decrease in polarity of sunscreen gels that affect the delocalization of the molecule and resulted in a rise of energy demand needed for excitation to happen and hence, increase the SPF value.

Conclusion

Addition of arbutin and olive oil affect the physical appearance (organoleptic and consistency) of sunscreen product as well as its spreading ability but has no effect on pH; while the significant raise in SPF value of the sunscreen formula showed that the addition of arbutin and olive oil affect the effectiveness of sunscreen product and an increase in olive oil concentration has lead to an increase in SPF.

Acknowledgement

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