Development of Novel Polymeric Sunscreen Agent

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Abstract

A novel polymeric sunscreen agent was developed. It was prepared by the coupling reaction of 2-ethylhexyl 4-hydroxycinnamate with poly vinylbenzyl chloride(PVBC, average MW: 6,500). In this reaction the reactivity was mostly affected by catalyst. In the absence of catalyst the yield was approximately 55% and in the presence of tetrabutylammonium bromide the yield was about 65%, but in the presence of tetrabutylammonium iodide the yield was 100% to give a average molecular weight 20,000 polymeric sunscreen agent. There were no side reactions, and its structure and purity were confirmed by various analytical methods, such as NMR, IR, and so on. UV radiation absorption efficiency is more than 70% compared with that of octyl methoxycinnamate. The solubility in polar oil, for example $C_{12\sim15}$ alkylbenzoate and caprylic/capric triglyceride, is more than 50%. It showed high stability in the time course of test including acceleration test. This polymer is safe to skin because of poor permeability to skin, no side products in the process of preparing, and easy elimination of excess starting materials.

Introduction

The ultraviolet ray exhibits injurious effects to life and cosmetic formulations. Repetitive sun exposure can result in skin changes known as photoaged skin. The clinical changes that are seen in photoaged skin differ from those of normally aged skin in some protected sites. There is increased wrinkling, elastosis, solar comedones, pigmentary changes, and precancerous and cancerous skin lesions. [1] In the United States alone 500,000 new cases of skin cancer are reported each year. [2] Also, the ultraviolet ray is the cause of decomposition and deterioration of cosmetic formulations. So, sunscreen agent became essential component in the cosmetic formulations. The ultimate sunscreen agents should have following characteristics.

1. Should be nontoxic, nonphototoxic and nonsensitizing
2. Absorb radiation in the UV region 280~360 nm and possess a large extinction coefficient (ε) at the wavelength (λ_{max}) at which it absorbs maximum UV radiation.
3. Should be stable to UV, high temperature
4. Should be compatible with cosmetic vehicles and ingredients and easy to use. [3]

Since sunscreen agents are believed irritant in cosmetics, it is important to develope materials safe to skin. The goal of this research is developing a sunscreen agent safe to skin. In view of skin toxicology, the safety factor to skin chiefly depends on the chemical structure of sunscreen agent and percutaneous absorption. [4] Throughout this study, we introduce a novel polymeric sunscreen agent which is very stable and safe to skin because of skin impermeability.

Experimental Part

TLC analysis was performed on Merck silica gel 60 F-254 plates and visualized by using an ultraviolet lamp and/or by spraying with 50% aqueous sulfuric acid and ethanolic phosphomolybdic acid and charring on a hotplate. IR spectra were recorded on a Perkin-Elmer 781 spectrophotometer. ^{1}H NMR spectra were recorded in $CDCl_3$ on JEOL GSX 270 and Brucker ARX 300 spectrophotometer. Chemical shifts were reported in parts per million relation to internal tetramethylsilane. UV spectra were recorded on a Varian Cary 4E and Perkin-Elmer Lambda 16. GPC analyses were performed on a system consisting of a Hewlett-Packard 1050 liquid chromatography and Waters HR 3 column. The reagents were all of reagent grade and used with further purification when necessary. 1) Polymerization of vinylbenzyl chloride A solution of freshly distilled vinylbenzyl chloride (4) 5g (6.55mmol) and azobis (isoburyronitrile) (AIBN) 0.054g (0.33mmol) in distilled benzene (50ml) was refluxed under N_2 for 2 days. The reaction mixture was diluted with distilled water (50ml) and left to stirred for 30 minutes and benzene layer was separated. The organic layer was dried over anhydrous $MgSO_4$ and concentrated. The crude product contained polymerized vinylbenzyl chloride (poly vinylbenzyl chloride, PVBC) and unreacted vinylbenzyl chloride (monomer). The crude product was dissolved in tetrahydrofuran (THF) (10ml). Then, n-hexane (25ml) was added to THF solution. Unpolymerized vinylbenzyl chloride was dissolved in solvent, but PVBC was precipitated and separated to give 2.9g (58%) as high viscous liquid. The average molecular weight was 6,500 according to GPC. ^{1}H-NMR ($CDCl_3$, 300MHz) d 6.3-7.2 (m, 4H, *arom*), 4.3-4.6 (m, 2H, ArCH_2Cl), 1.3-2.0 (m, 3H, Ar$CHCH_2$). IR 2800, 1600, 1440, 1250, 695cm^{-1}.
2) 2-ethylhexyl 4-hydroxycinnamate (3) A solution of 4-hydroxycinnamic (5)acid 5g (50mmol) and 2-ethylhexyl alcohol (6) 9.75g (75mmol) and p-toluenesulfonic acid 0.2g in distilled benzene (50ml) was refluxed with Dean-Stark apparatus for 24 horus. After cooling to room temperature, aqueous sodium bicarbonate was added and stirred for 1

hour. The organic layer was dried over anhydrous $MgSO_4$ and concentrated *in vacuo*. The crude product was chromatographed on a silica gel eluting CH_2Cl_2 to give 7.0g (85%) as coloress liquid. ^{1}H-NMR ($CDCl_3$, 300MHz) δ 6.85, 7.35 (m, 4H, *arom*), 6.3, 7.65(dd, 2H, ArC*H*C*H*CO-)5.25 (s, 1H, ArO*H*) 4.1 (d, 2H, OCH_2alkyl), 0.9-1.7 (m, 15H, *alkyl*). IR 3600-3100 (broad, OH), 2950, 1670, 1630, 1600, 1500, 1430, 1360, 1200, 1220, 830cm^{-1}. 3) Polymeric sunscreen agent (7) A solution of PVBC 2.0g (13meq), anhydrous potassium carbonate 3.6g (26mmol), tetrabutylammoniumiodide (TBAI) 0.2g and 2-ethylhexyl 4-hydroxycinnamate (3) 2.6g (15.6mmol) in acetone (50ml) was refluxed for 16 hours. After cooling to room temperature, distilled water (50ml) was added and stirred for 30 minutes and acetone was removed *in vacuo*. The mixture was then extracted with CH_2Cl_2, and the extract was washed with water, dried ($MgSO_4$), and concentrated. The crude product was dissolved in THF (10ml). Then, n-hexane (25ml) was added to THF solution. Undissolved polymer was separated and dried *in vacuo* to give the polymeric sunscreen agent 3.5g (93%). ^{1}H-NMR ($CDCl_3$, 300MHz) δ 6.4-7.5 (m, 8H, *arom*), 6.2-6.4, 7.5-7.7 (m, 2H, ArC*H*C*H*CO-), 4.6-4.9 (m, 2H, ArCH_2OAr), 4.0-4.2 (m, 2H, OCH_2alkyl), 0.8-1.7 (m, 18H, *alkyl*). IR 2920, 1710, 1600, 1510, 1250, 1160 cm^{-1}. 4) Solubility Test Polymeric sunscreen agent was added to C12~15 alkylbenzoate, caprylic/capric triglyceride and stirred 5,000 rpm by Polytron (PT 3000) at 80 °C for 10 minutes. After cooling to room temperature, the solution was left for 24 hours and centrifuged at 13,000 rpm for 2 minutes. The solubility was determined by direct observation.

5) Cosmetic formulation containing polymeric sunscreen agent. Cosmetic formulation containing polymeric sunscreen agent was as followed.

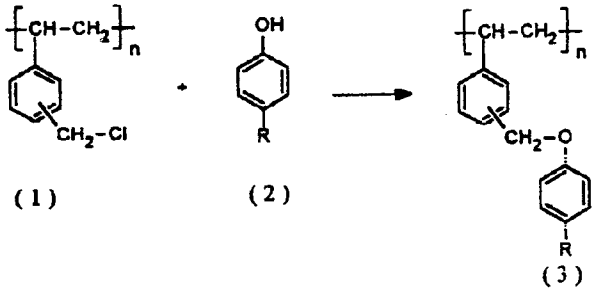
	1	2	3	4	5
Stearic Acid	1.5	1.5	1.5	1.5	1.5
Cetearyl Alcohol	2.0	2.0	2.0	2.0	2.0
Glyceryl Monostearate	1.0	1.0	1.0	1.0	1.0
Glyceryl Stearate and PEG-100 Stearate	1.0	1.0	1.0	1.0	1.0
Mineral Oil	-	-	-	3.0	3.0
Caprylic/capric Triglyceride	18	15	15	15	15
Octyl Methoxy Cinnamate	-	3	-	3	-
Polymeric Sunscreen Agent	-	3	-	3	-
PEG-40 Stearate	1.5	1.5	1.5	1.5	1.5
Sorbitan Stearate	0.5	0.5	0.5	0.5	0.5
Propylene Glycol	7.0	7.0	7.0	7.0	7.0
Tri Ethanol Amine	1.5	1.5	1.5	1.5	1.5
Deionized Water	to 100	to 100	to 100	to 100	to 100

6) SPF measurement [5]: SPF-290/S analyzer <Optometrics, USA>

Results and Discussion

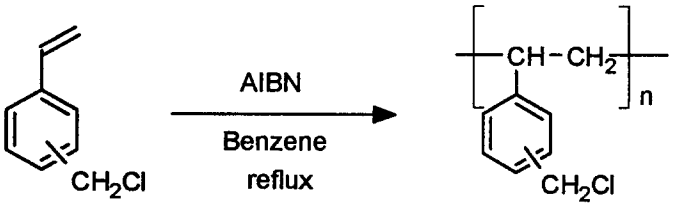
The reaction of PVBC and phenolic compounds was generally known for a long time. [6]

Scheme I



In this research, the unit of octyl methoxycinnamate was reacted with PVBC to give polymeric sunscreen agent. PVBC was prepared by the free radical polymerization of vinylbenzyl chloride initiated by AIBN. The average molecular weight was largely controlled by the amount of AIBN. The amount of AIBN was 1/20~1/30 compared to vinylbenzyl chloride to give a average molecular weight 6,000 ~ 7,000 polymer.

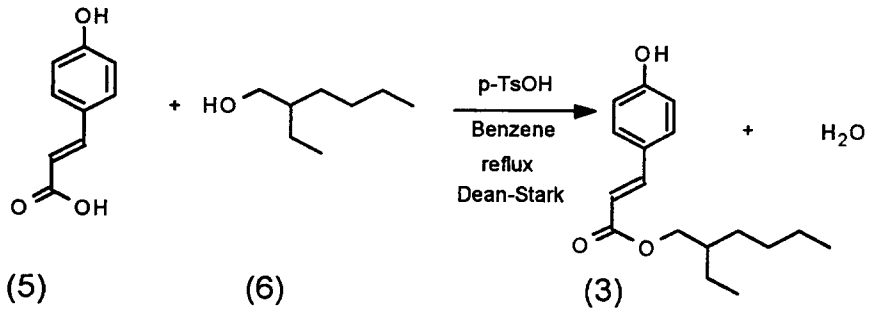
Scheme II



(4) (1)

The reaction of 4-hydroxycinnamic acid and 2-ethylhexyl alcohol gave 2-ethylhexyl 4-hydroxycinnamate

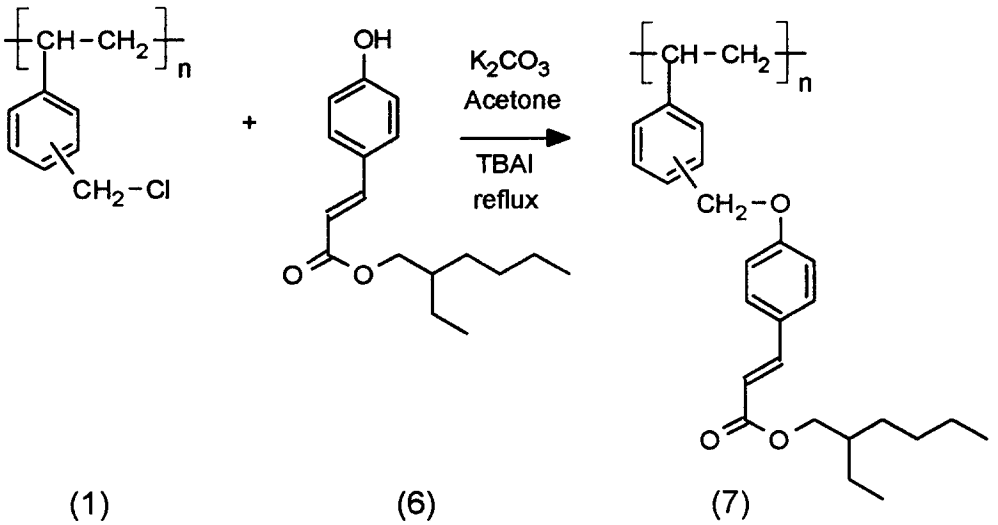
Scheme III



(5) (6) (3)

The polymeric sunscreen agent was obtained by the reaction of PVBC and 2-ethylhexyl 4-hydroxycinnamate.

Scheme IV



(1) (6) (7)

In the reaction of PVBC and nucleophilic reagents, the relation of reaction yield and phase transfer catalyst (PTC) were reported. [7] In case using PTC, the reaction yield was remarkably improved. In the absence of PTC the conversion yield (benzyl chloride carbon to benzyl ether carbon) was approximately 55% and in the presence of PTC (tetrabutylammonium bromide) the yield was about 65%, but in the presence of PTC (tetrabutylammonium iodide) the yield was 100%. The conversion yield was determined by NMR spectra. PVBC exhibits the signal of benzylic chloride proton around 4.3ppm. The polymer which benzylic chloride completely conversed to sunscreen agent exhibit the signal of benzylic ether proton around 4.7ppm. Shown NMR spectra the polymer in this study showed no signal around 4.3 ppm.

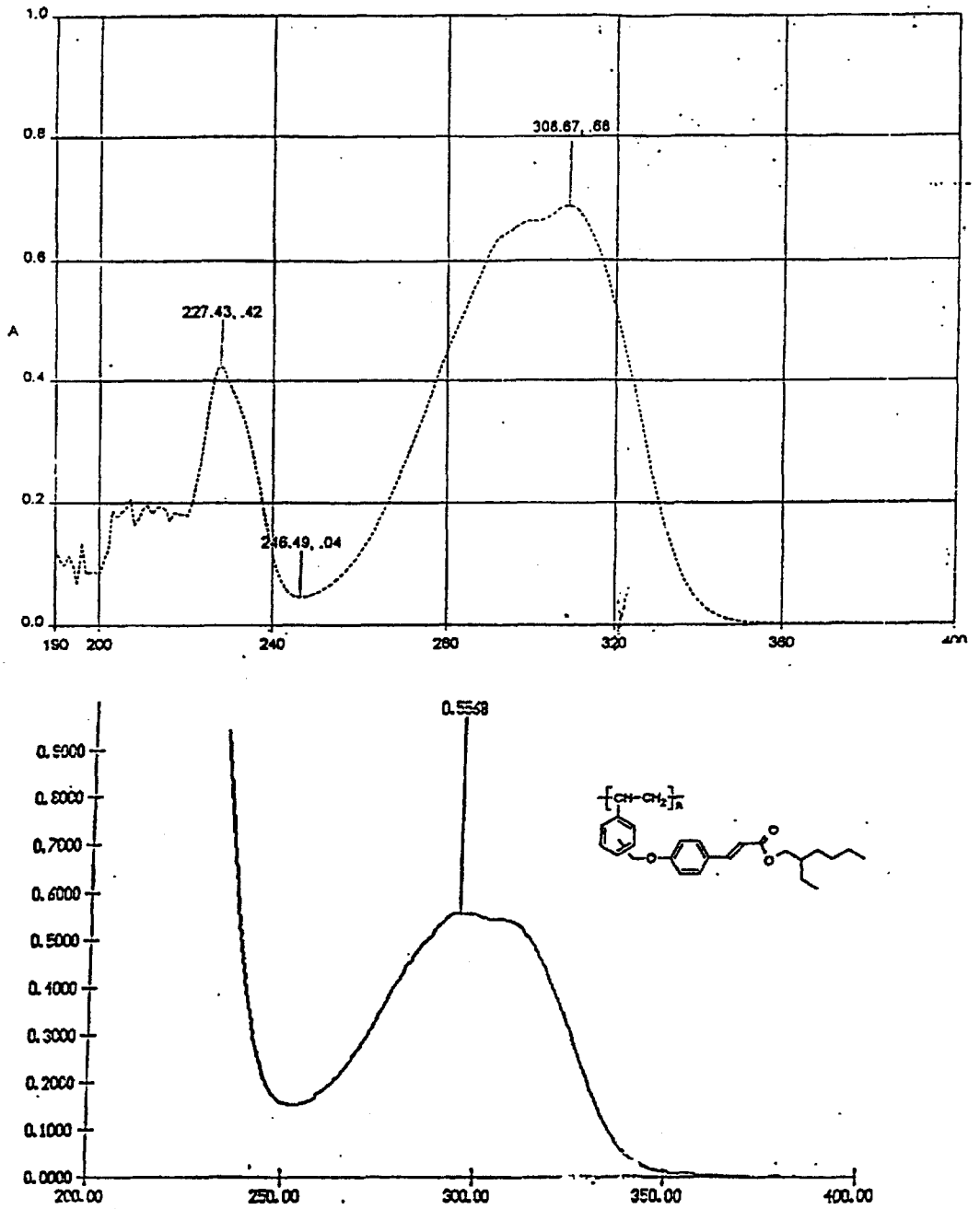


Figure 1. UV spectrum of octyl methoxycinnamate (above), polymeric sunscreen agent (below), 8.26 ppm , solvent : methylene chloride

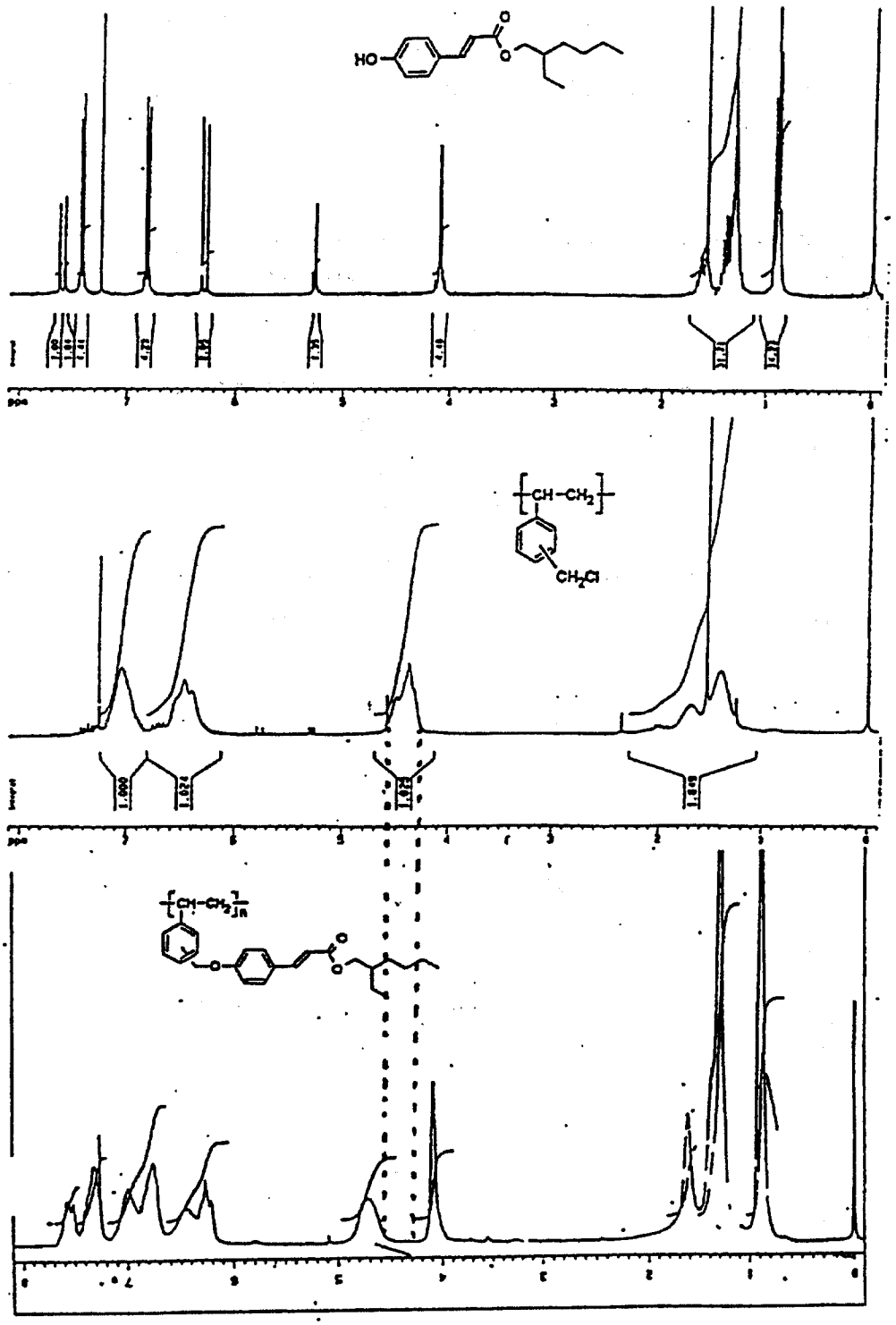


Figure 2. NMR spectrum (solvent : $CDCl_3$) of 2-ethylhexyl 4-hydroxycinnamate (above), PVBC (medium), polymeric sunscreen agent (below)

The size of polymers were determined by the GPC. The data obtained from the GPC of PVBC and polymeric sunscreen agent were compared with that of polystyrene molecular weight standard materials. The average molecular weight of PVBC and polymeric sunscreen agent were 6,000 ~ 7,000 and 20,000.

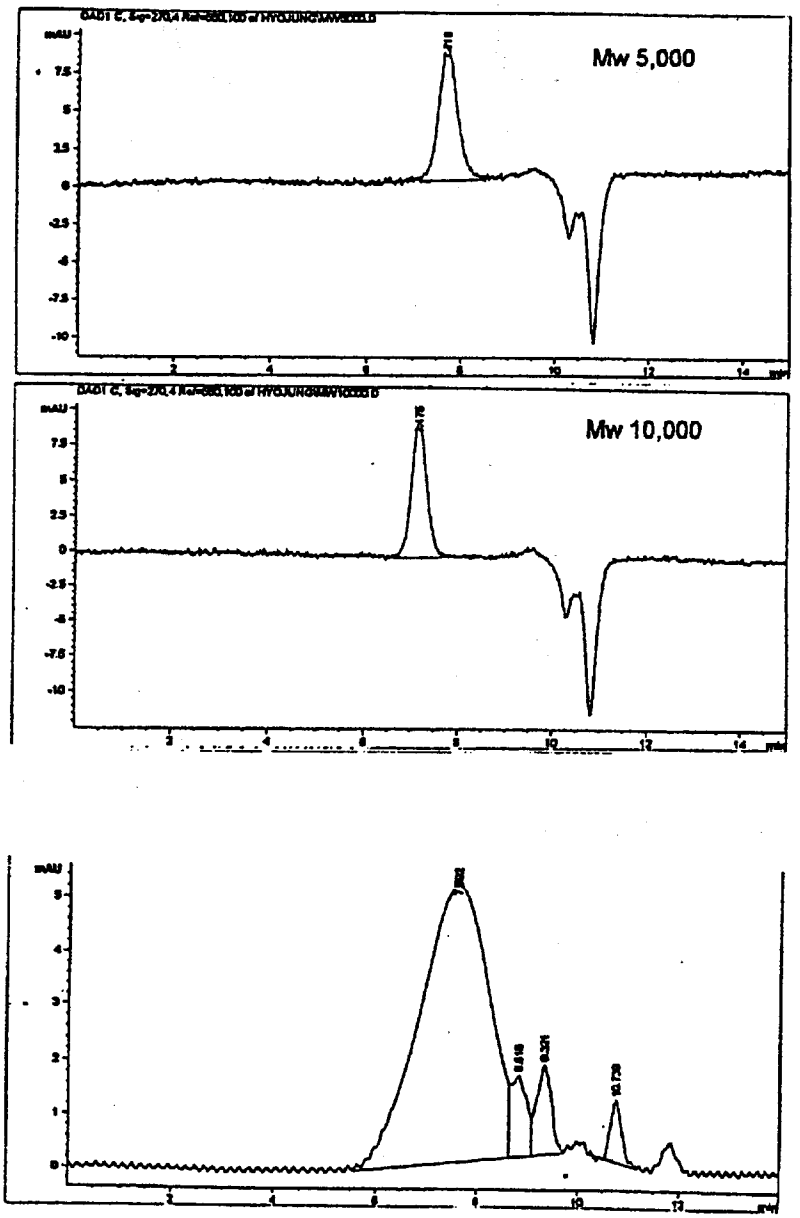
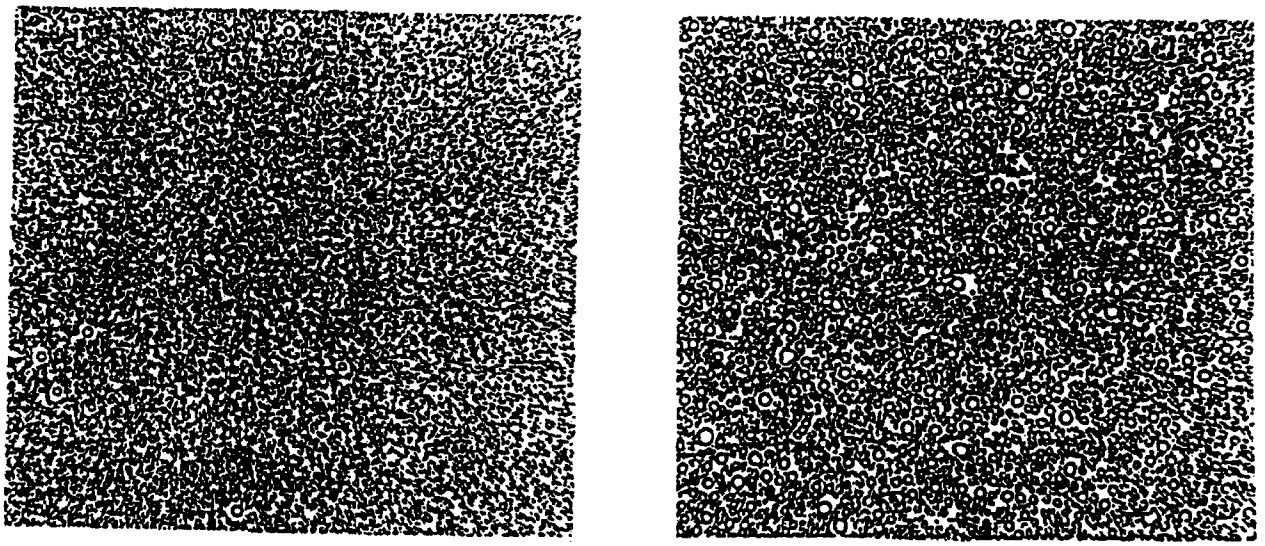


Figure 3. GPC result of polystyrene MW Standard (above), PVBC (below)

(Waters HR 3 column, Hewlett Packard 1050 system)

The solubility of polymer was tested for two cosmetic polar oil. (C12~15 alkyl benzoate, caprylic/capric triglyceride) The polymeric sunscreen agent showed above 50% solubility to both oil. The cosmetic formulation containing polymeric sunscreen agent showed similar characteristics compared with the formulation containing octylmethoxycinnamate or caprylic/capric triglyceride instead of polymeric sunscreen agent.
Fig. 4 showed microscopic photograph of O/W emulsion containing polymeric sunscreen agent and control



No. 2 No. 3

Figure 4. The microscopic photograph of formula No. 2,3

The SPF of cosmetic formulation containing polymeric sunscreen agent was 70% compared with formulation containing octyl methoxycinnamate. The molecular weight of a unit of the polymer is 392 and that of octyl methoxycinnamate is 290. The UV absorption of the polymer compared with that of octyl methoxycinnamate is 74% since the unit of polymer is chemically based on octyl methoxycinnamate. The SPF of cosmetic formulation containing 3% polymeric sunscreen agent was 3.7 and the formulation containing 3% octyl methoxycinnamate was 5.3

Conclusion

The polymeric sunscreen agent in this research has several excellent advantages as cosmetic materials.
1) It is very safe material because it can't permeate to skin.
2) The solubility to cosmetic polar oil is far more than 50%.
3) The SPF of cosmetic formulation containing polymeric sunscreen agent was above 70% compared with formulation containing octyl methoxycinnamate.
4) It is easy to prepare without any contaminants.
Therefore the new polymeric sunscreen agent covers a problem that present sunscreen agents have in safety, it is very desirable cosmetic raw material.

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Note : The references have been scanned to maintain character set.