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Effects of Polyols on Antimicrobial and Preservative Efficacy in Cosmetics

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요 약: 일반적으로 화장품에는 제품의 보존성을 향상시키는 것을 목적으로, 파라옥시안식향산에스텔(paraben, 파라벤), 이미다졸리디닐우레아, 페녹시에탄올, 클로로페네신 등의 화학 방부제가 배합되어 있다. 화학 방부제는 제형의 안정성 및 방부 유효성이 우수하지만, 독성, 피부자극, 알러지를 유발하는 등의 단점이 있어 배합량을 줄이거나 배제하고도 제품의 안정성 및 유효성이 높은 보존 기술이 요구된다. 종래부터 글리세린, 1,3-부틸렌글리콜(BG), 프로필렌글리콜(PG), 디프로필렌글리콜(DPG) 등의 폴리올류들은 보습성분 및 용매로 범용되고 있으며, 고농도로 사용할 경우 항균력이 있지만, 사용성을 떨어뜨리고, 피부 자극을 유발하는 등 제품의 성능을 저하시키는 문제점이 있었다. 본 연구의 목적은 폴리올류의 조성별 항균, 방부력 영향을 평가하고, 스킨케어 유화 제형에서 방부제 함량을 감소시킬 수 있는 폴리올 조성을 도출하여 방부제의 사용량을 감소시키고, 사용성 및 안정성도 개선하는 것이다. 범용적으로 사용되는 폴리올류의 항균 증가력을 측정한 결과 글리세린의 항균 증가력은 미미한 반면 BG, PG의 영향력은 유의($p < 0.05$) 하였다. *S. aureus*를 대상으로 화학 방부제의 항균력 증가를 측정하고 상관성을 회귀분석한 결과 폴리올 1 %를 증량할 때 PG는 2.1 ~ 8.4 %, BG는 1.8 ~ 8.4 % 방부제의 항균력을 증가시킬 것으로 추정되었다. 로션, 크림 등 유화제품에서 폴리올에 의한 방부력 증가율을 측정한 결과 글리세린의 경우 5 %까지 함량을 증가시켜도 방부력이 증진되지 않았으며, BG 및 PG는 5.5 ~ 9.9 % 증가할 때 40 % 이상까지 방부력을 증가시켰다. 이상의 폴리올의 항균, 방부 영향력 측정으로 유화 제품에서 폴리올 배합을 조정하여 방부제 사용량을 40 %까지 감소시키고 사용성과 안전성 그리고 제품의 안정성을 개선할 수 있음을 확인하였고, paraben-free, 저방부, 무방부 시스템 도입시 베이스 처방의 기준으로 활용할 수 있을 것으로 기대된다.

Abstract: It is inevitable to use germicidal agents like parabens, imidazolidinyl urea, phenoxyethanol and chlorphenesin to preserve the cosmetics. Although effective in reducing microbiological contamination, chemical preservatives are irritative, allergenic and even toxic to human skin. So it is needed to decrease or eliminate usage of preservatives in cosmetic products. Glycerin, butylene glycol (BG), propylene glycol (PG), and dipropylene glycol (DPG) are widely used in cosmetics as skin conditioning agent or solvents. At high concentrations, they have antimicrobial activities, but deteriorate product quality like sensory feeling or safety. The purpose of study is to evaluate the effects of polyols on antimicrobial and preservative efficacy and confirm whether using adjusted polyols can decrease the contents of preservatives without deterioration of the quality of cosmetics. Effects of common polyols on antimicrobial activities of general preservatives were measured. BG and PG significantly ($p < 0.05$) increased activities of preservatives, but glycerin influenced little. It was inferred from the regression analysis of the results with *S. aureus* that adding 1 % of PG increased activities of preservatives up to 2.1 ~ 8.4 % and BG improved activities of preservatives up to 1.8 ~ 8.4 %. The challenge test results for oil in water lotions and creams showed that BG and PG improved the efficacy of preservative systems up to 40 % at a range of 5.5 ~ 9.9 %, but glycerin had little effect on it. The measured rates of improvement were analogous to the inferences from regression analysis. It can be concluded that is possible to reduce total chemical preservatives up to 40 %, consequently improve the safety and sensory quality of cosmetics with the precision control of polyols. Added to that, using this paradigm, low preservative contents, praraben-free system, and even preservative-free systems can be expected in the near future.

Keywords: *polyol, preservative, antimicrobial, preservative efficacy, germicidal*

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1. Introduction

The term preservation will be limited to the protection of cosmetics, toiletries, and drugs from the effects of microbiological contamination. It is inevitable to use germicidal agents like parabens, imidazolidinyl urea, phenoxyethanol (PE) and chlorphenesin (CPN) to preserve the cosmetics. Unfortunately there is more to the story, since in many cases chemicals which are highly active against microbes also have similar effects against mammalian cells. Although effective for microbiological contamination, chemical preservatives are irritative, allergenic and even toxic for human skin. Therefore a balance needs to be established with the preservative of choice between killing organisms which may be in the cosmetic and injuring cells of the consumer who uses the product. In addition, there are a host of variables in the finished product which influence the effectiveness of preservatives active in laboratory media. Predictions of preservative strength based on information gained from laboratory growth media cannot be extrapolated to complex cosmetic formulae without rigorous testing. Microbial contamination of cosmetic, toiletries, and pharmaceuticals is of grave concern to industry, regulating agencies, and the person most affected-the consumer. So it is needed to decrease or eliminate preservatives in cosmetic products. Glycerin (Gly), butylene glycol (BG), propylene glycol (PG)[1], dipropylene glycol (DPG)[2] are widely used in cosmetics as skin conditioning agent or solvents. At high concentration, they have antimicrobial activities[3,4], but deteriorate product quality like sensory feeling or safety[5,6].

2. Materials and Methods

2.1. Polyols

Glycerin, 1,3-butylene glycol, propylene glycol and dipropylene glycol were purchased from Sigma-Aldrich (Korea).

2.2. Preservatives

Methylpraraben (MP), propylparaben (PP), phenoxyethanol and chlorphenesin were used as preservatives.

Table 1. MIC of General Polyols (%)

Strains	Gly	BG	PG	DPG
E. coli[1)]	28	10	10	8
P. aeruginosa	40	10	10	10
S. aureus	35	14	16	14
C. albicans	30	10	14	14
A. niger	40	14	16	18

1) *E. coli*: *Escheria coli*, *P. aeruginosa*: *Pseudomonas aeruginosa*, *S. aureus*: *Staphylococcus aureus*, *C. albicans*: *Candida albicans*, *A. niger*: *Aspergillus niger*

2.3. Microorganisms

S. aureus (Sa, Gram-positive) ATCC 6538, *E. coil* (Ec, Gram-negative) ATCC 8739, *P. aeruginosa* (Pa, Gram-negative) ATCC 9027 were used as bacterial strains and *C. albicans* (Ca, yeast) ATCC 10231 and *A. niger* (An, mold) ATCC 16404 were used as yeast and mold strains for antimicrobial and preservative efficacy tests.

2.4. Antimicrobial Tests

Antimicrobial tests were performed by broth dilution method to decide the minimal inhibitory concentration (MIC). Tryptic soy broth and sabauroud dextrose broth were used for culture media of bacteria and yeasts/mold, respectively. The MICs were decided after 48 h after inoculation for bacteria at 32 ℃, and at 25 ℃ and for 72 h for yeast/mold.

2.5. Preservative Efficacy Tests

Preservative efficacy tests (challenge tests) were performed by CTFA guidelines for O/W emulsion products.

2.6. Statistics

Statistical analyses were carried out by Minitab 14 program.

3. Results and Discussion

3.1. Antimicrobial Activity of General Polyols

Enough preservative activity was expected at the concentration above 40 %, 14 %, 16 % and 18 % of Gly, BG, PG and DPG, respectively (Table 1).

Table 2. Antimicrobial Enhancement Power for Yeast and Mold, (MIC ratio) = (control MIC) / (sample MIC)

Polyol (%)			*C. albicans*[1]			*A. niger*[2]		
Gly[3]	BG	PG	MP[4]	CPN	PE	MP	CPN	PE
0	0	0	1	1	1	1	1	1
2	2	2	1	1.125	1.5	1	0.8571	1.25
6	2	2	1	1.286	1.8	1	0.8571	1.25
2	6	2	1.667	2.25	3	1.5	1.2	2.5
6	6	2	2.5	3	3	3	1.5	5
2	2	6	1.25	1.8	3	1	1	2.5
6	2	6	1.667	1.8	3	1.5	1.2	2.5
2	6	6	> 20	> 3.6	> 9	> 12	> 2.4	> 5
6	6	6	> 20	> 3.6	> 9	> 12	> 2.4	> 5
4	4	4	1.25	1.8	4.5	0.75	1.2	2.5

1) *C. albicans*: *Candida albicans*
2) *A. niger*: *Aspergillus niger*
3) Gly: glycerin, BG: butylene glycol, PG: propylene glycol
4) MP: methyl paraben, CPN: chlorophenesin, PE: phenoxyethanol

Table 3. Antimicrobial Enhancement Power for Bacteria, (MIC ratio) = (control MIC) / (sample MIC)

Polyol (%)			*P. aeruginosa*[1]			*S. aureus*[2]	
Gly[3]	BG	PG	MP[4]	CPN	PE	CPN	PE
0	0	0	1	1	1	1	1
2	2	2	1.1	1	1.29	1	1
6	2	2	1.1	1	1.5	1	1
2	6	2	> 5.5	> 16	> 9	1.17	1
6	6	2	> 5.5	> 16	> 9	1.17	1.08
2	2	6	> 5.5	> 16	> 9	1.17	1.08
6	2	6	> 5.5	> 16	> 9	1.17	1.08
2	6	6	> 5.5	> 16	> 9	1.17	1.4
6	6	6	> 5.5	> 16	> 9	1.4	1.4
4	4	4	> 5.5	> 16	> 9	1.17	1.08

1) *P. aeruginosa*: *Pseudomonas aeruginosa*
2) *S. aureus*: *Staphylococcus aureus*
3) Gly: glycerin, BG: butylene glycol, PG: propylene glycol
4) MP: methyl paraben, CPN: chlorophenesin, PE: phenoxyethanol

3.2. Influence of Polyol Compositions on Antimicrobial Activity

Influences of polyol compositions on antimicrobial activity were illustrated in Table 2 and Table 3 for bacteria and yeasts / mold, respectively.

Regression analyses were performed and coefficients of each polyol for regression equations were calculated by Minitab program (Table 4).

Regression Equation
Enhancement ratio = Constant + aGly (%) + bBG (%) + cPG (%). (1)

In most cases, the R-square value of analysis was shown good correlations above 70 % (Table 4), except *C. albicans* (MP). The respective antimicrobial activity of MP, PE and CPN was significantly enhanced by BG and PG ($p < 0.05$), while the antimicrobial enhancement power of glycerin was negligible. The inherent antimicrobial activity and enhancement of antimicrobial activity of BG was slightly superior to PG against yeasts and molds but similar against bacteria (the data of antimicrobial activity on *S. aureus* was excluded).

Gram-positive *S. aureus* was selected as the critical microbe to evaluate preservative efficacy of MP, CPN and PE, because it is strongly resistant to those preservatives. It was expected that the antimicrobial activity of MP, CPN and PE would be enhanced to 2.1 %, 8.4 % and 6.0 % by addition of 1 % PG and to 1.8 %, 8.4 %, 4.6 % by addition of 1 % BG, respectively.

3.3. Influence of Polyol Compositions on Preservative Efficacy

Influences of polyol compositions on preservative efficacy were showed in Table 5. More than 40 % enhancement of preservative efficacy was observed in BG and PG groups in the concentrations between 5.5 ~ 9.9 %. PG was most effective, followed by BG while no enhancement of preservative efficacy was shown in glycerin to the concentrations of 6.2 %. Most experimentally measured enhancement rate of preservative efficacy was similar to the expected value using regression equation (Equation 1, Table 4). Particularly in the formula of cream 2, enhancement rate of preservative efficacy derived by polyol was exceeded the expected value by more than 2 times. It is considered that the preservative efficacy would be severely affected by extreme change of partition coefficient as polyol increased, for cream 2 contains high contents of polar oil such as octyldodecanol (3 %) and cetyl ethylhexanoate (3 %).

Table 4. Regression Analysis (Coefficients)

Strain[1)]	Preservatives[2)]	Constant	a	b	c	R-Sq (%)
Ca	CPN	0.424	0.0356	0.3172	0.0985	83.1
Ca	MP	0.524	0.0615	0.1681	0.0467	66.7
Ca	PE	0.534	-0.0009	0.319	0.3192	81
An	CPN	0.255	-0.0132	0.1927	0.1257	77.3
An	MP	-4.524	-0.126	1.228	1.0618	61.4
An	PE	-0.407	0.0455	0.5145	0.3064	80.9
Sa	CPN	0.748	0.0219	0.0844	0.0844	86.7
Sa	MP	0.98	0.0043	0.0178	0.0206	97.7
Sa	PE	0.694	0.0065	0.0463	0.0602	79.8
Pa	CPN	-3.507	-1.115	2.623	2.6231	90.7
Pa	MP	-0.29	-0.3203	0.7783	0.7784	91.2
Pa	PE	-1.207	-0.5158	1.3588	1.3592	91.4

1) *Ca: Candida albicans, An: Aspergillus niger, Pa: Pseudomonas aeruginosa, Sa: Staphylococcus aureus*
2) MP: methyl paraben, CPN: chlorophenesin, PE: phenoxyethanol

Table 5. Enhancement Effects of Polyols on Preservative

Product	Preservatives[1)]	Polyol[2)]	Polyol Increase (%)	Predicted (%)[3)]	Measured (%)
O/W Cream 1	CPN	BG	6.4	53.7	40
		PG	6.4	53.7	60
O/W Cream 2	PE	BG	5.5	25.3	> 62.5
		PG	5.5	33	> 62.5
O/W Lotion 1	PE	BG	9.9	45.6	40
		PG	9.9	59.5	80
		Gly	6.2	4	0
O/W Lotion 2	CPN	BG	5.8	48.7	< 40
		PG	5.8	48.7	40

1) CPN: chlorophenesin, PE: phenoxyethanol
2) BG: butylene glycol, PG: propylene glycol, Gly: glycerin
3) Predicted enhancement effects were calculated by regression equation (Equation 1)

4. Conclusions

1) Regarding to the result of antimicrobial activity assay of polyols, it is needed to use at least of glycerin 40 %, BG 14 %, PG 16 %, and DPG 18 % of the concentration for sole preservative.

2) The respective antimicrobial activity of MP, PE and CPN was significantly enhanced by BG and PG ($p < 0.05$), while the enhancement of antimicrobial activity by glycerin was negligible. BG was superior to PG in antimicrobial activity.

3) It was expected that the preservative efficacy was enhanced to MP 2.1 %, CPN 8.4 %, and PE 6.0 % by addition of PG 1 % and to MP 1.8 %, CPN 8.4 %, and PE 4.6 % by addition of 1 % BG, respectively, at the concentration of polyol below 10 %.

4) More than 40 % enhancement of preservative efficacy was observed in BG and PG. PG was most effective, followed by BG while no enhancement of preservative efficacy was shown in glycerin to the concentrations to 6.2 %.

5) Most experimentally measured enhancement rate of preservative efficacy was similar to the expected value using regression equation, considering intervals of test sample concentration and reliability of test. And there were some exceptional results affected by change

of partition coefficient caused by polyol increase.

As the results described above, preservative efficacy of 4 emulsion products (cream and lotion) was improved above 20 % by adjusting the composition of polyols. Those results are expected to be applied to the standardization of base formula of paraben-free, low-preservative and non-preservative cosmetics.

References

1. I. Olitzky, Antimicrobial properties of a propylene glycol based topical therapeutic agent, *J. Pharm Sci.*, **54**(5), 787 (1965).
2. T. Kinnunen and M. Koskela, Antibacterial and antifungal properties of propylene glycol, hexylene glycol and 1,3-butylene glycol *in vitro*, *Acta Derm. Venereo.*, **71**(2), 148 (1991).
3. Z. Gruntova and S. Thurzova, Effect of glycerin and propylene glycol on microbial contamination of some o/w ointment bases, *Cesk. Farm.*, **20**(8), 299 (1971).
4. P. A. Thomas, K. S. Bhat, and K. M. Kotian, Antibacterial properties of dilute formocresol and eugenol and propylene glycol, *Oral. Med. Oral Patho.*, **49**(2), 166 (1980).
5. D. I. Williamson and G. Russell, Ethylene glycol as a preservative for marine organisms, *Nature*, **206**(991), 1370 (1965).
6. R. M. Darwish and S. F. Bloomfield, Effect of ethanol propylene glycol and glycerol on the interaction of methyl and propyl *p*-hydroxybenzoate with *Staphylococcus aureus* and *Pseudomonas aeruginosa*, *Int. J. of Pham.*, **147**, 51 (1997).