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Antibacterial and Antifungal Properties of Propylene Glycol, Hexylene Glycol, and 1,3-Butylene Glycol In vitro

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The antimicrobial properties of three glycols, – propylene glycol, hexylene glycol, and 1,3-butylene glycol – against Candida albicans, Staphylococcus aureus, Staphylococcus epidermidis, Streptococcus pyogenes A, Streptococcus mitis, and E. coli were studied in vitro. Within 20 h, 10% and 30% hexylene glycol in fresh tryptic soy broth were able to kill all the micro-organisms listed above. Five percent hexylene glycol showed some antimicrobial properties but the 1% agent had no effect. Thirty percent 1,3-butylene glycol and 30% propylene glycol were approximately as effective as 10% HG. The results speak in favour of using hexylene glycol in cosmetic and dermatological vehicles instead of propylene glycol and 1,3-butylene glycol.

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Propylene glycol (PG) is widely used as a humectant, an antimicrobial agent, and as a solvent in many dermatological vehicles and in cosmetic skin care and hair care products (1–3). PG has an irritant effect on the skin, which is quite evident as increased water loss especially in atopics (4), and it is also a sensitizer (4–7).

Hexylene (HG) and 1,3-butylene glycols (BG) are also used in cosmetic products in concentrations ranging from 0.1% to 50% as humectants, antimicrobial agents, and solvents (8). HG is used in at least one commercially available corticosteroid ointment (Legederm® ointment, Schering Corporation, Kenilworth, New Jersey, USA). Undiluted HG – but not a 25% solution – has been found to irritate rabbit skin (8–9). In repeated open application tests, HG did not irritate human skin, and under occlusion it was less irritating than PG (4). The moisturizing properties of PG and BG are similar (1, 10). They are nearly five times more hygroscopic than HG (1). BG is considered to be the best antimicrobial agent among these three glycols (11), HG being the second best (2). According to the CIR Panel, these glycols had low toxity in acute, subchronic and chronic oral toxity studies using a variety of animal species (9).

The aim of the present study was to investigate the antimicrobial properties of PG, HG, and BG against Candida albicans and certain pathogenic and non-pathogenic bacteria.

MATERIALS AND METHODS

Staphylococcus aureus (ATCC 29213), Staphylococcus epidermidis (ATCC 12228), Streptococcus pyogenes A, Streptococcus mitis, E. coli (ATCC 253221) and Candida albicans were used as test organisms.

1,3-butylene glycol, pro anal. (Fluka Chemie AG, Switzerland), propylene glycol (Tamro Oy, Finland, Ph. Eur.) and hexylene glycol, puriss (Fluka Chemie AG, Switzerland) were used as test substances. Bacto Tryptic soy broth (Difco Laboratories, Detroit, Michigan, USA) was used as the test medium. The minimal cidal concentration (MCC) was determined as follows: tubes with 10 ml of fresh tryptic soy broth with 0, 1, 5, 10 or 30 per cent of test substances (v/v) were inoculated with 100 µl of an overnight culture of the appropriate microorganism. The microbe concentra-

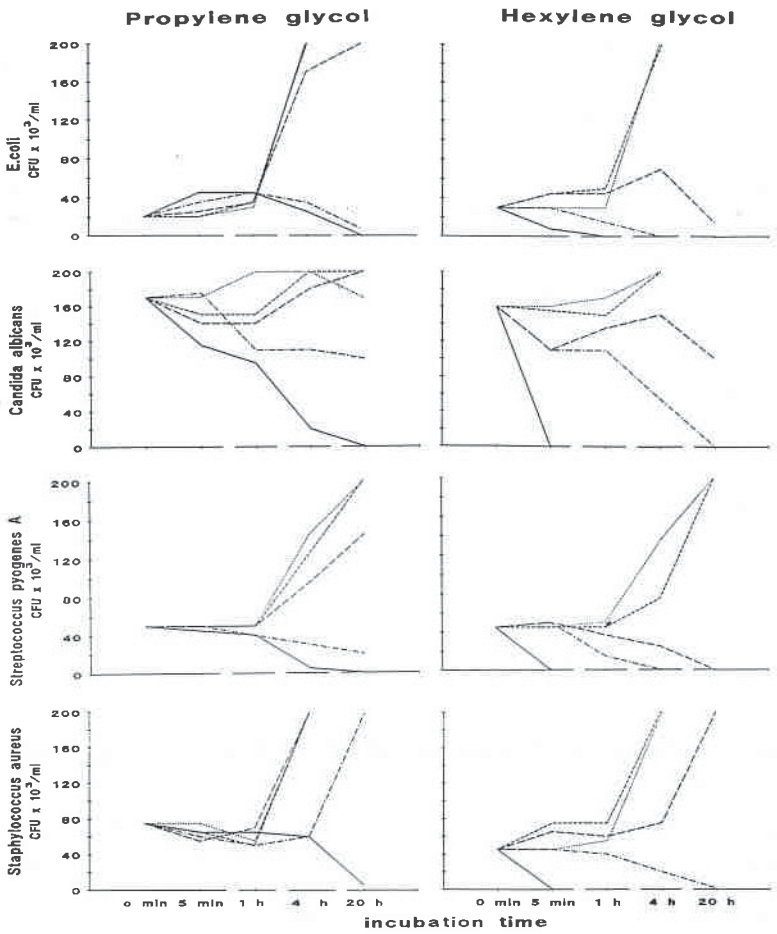

Fig. 1. The inhibition of the growth of E. coli and Candida albicans, and Streptococcus pyogenes A and Staphylococcus aureus, by propylene glycol, and hexylene glycol in soy broth. Overall, 10% hexylene glycol was as effective as 30% propylene glycol (and 30% 1,3-butylene glycol) in inhibiting at least 90% of the growth of microbes over 20

..... 0%
- - - - - - 1%
– – – – – 5%
. – – . 10%
——— 30%

tion in tryptic soy broth was approximately 10^6 CFU/ml (colony-forming units/ml). The tubes were incubated aerobically at +37°C for 20 h. The microbial growth was followed by subculturing a sample of 1 µl from each of the tubes on a blood agar plate immediately after adding the test organism to the medium; thereafter at 5 min, and at 1, 4 and 20 h during the incubation.

After overnight incubation of the plates at +37°C the number of colonies formed from each sample (CFU/ml) was calculated. All tests were carried out in triplicate.

RESULTS

All three glycols, PG, HG, and BG, proved antibacterial and antifungal at 30%. At lower concentrations, HG was more potent than BG and PG, the latter two having very similar antimicrobial properties. The MCC values of BG and PG for S.epidermidis and for Str. mitis equalled those for S. aureus and pyogenic streptococcus, respectively. In Fig. 1 the antimicrobial effects of PG and HG against Str. pyogenes A, S-aureus, E. coli and Candica albicans are shown.

DISCUSSION

In the present study, HG proved a more potent antimicrobial agent than BG and PG in vitro, a finding that agreed with that of Faergemann (2) who found HG better than PG, and with Faergemann & Frederiksson (12) who showed that the longer the carbon chain in glycol was, the better its antifungal effect. On the other hand, the finding of Harb & Toama (11) was that BG should be more effective than other polyols against common bacteria and yeasts.

Because HG is less irritating than PG to human skin (4), it would seem to be a very promising candidate for various dermatological formulations. The antibacterial and irritant properties of the ultimate

products containing HG might, however, differ from those achieved with aqueous solutions of HG.

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On the Putative Mechanism of Induction and Regulation of Melanogenesis by L-tyrosine

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The stimulation of melanogenesis by L-tyrosine in hamster melanoma is several-fold higher than that by norepinephrine, epinephrine, clonidine and isoproterenol and absent in the case of tyramine dopamine and phenylephrine. Therefore, the melanogenic effect of L-tyrosine in hamster melanoma follows a different pathway than that linked to the activation of dopaminergic and adrenergic receptors.

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L-tyrosine is a precursor for proteins, tyramine, catecholamines, melanin and thyroid hormones (1). In some pigmentary systems, L-tyrosine, besides its function as a precursor to melanin, can also act as an inducer and a regulator of the melanogenic apparatus (2–6). In cultured melanoma cells, L-tyrosine is converted to melanin, and can also be metabolized to catecholamines (5, 7). In addition, it has been reported that activation of adrenergic receptors can stimulate melanogenesis (8). We therefore decided to test whether the regulatory role of L-tyrosine in melanin synthesis is specific for this amino acid, or follows the pathway linked to the activation of dopaminergic or adrenergic receptors. As an experimental model for these studies, we used Bomirski amelanotic hamster melanoma cells, in which L-tyrosine can act as an inducer and regulator of the melanogenic apparatus (2, 6, 9, 10). The effect of L-tyrosine was found to be dose dependent (2), and apparently unrelated to pathways linked to cyclic AMP, cyclic GMP, or $InsP_3$ (11).

MATERIALS AND METHODS

L-tyrosine, tyramine, L-dopa, dopamine, L-phenylephrine, clonidine, (-)isoproterenol, (-)epinephrine, (±)norepinephrine were obtained from Sigma. L-(ring-3,5-^{3}H)-tyro-