Administration, Rm. 4–62, 5600 Fishers Lane, Rockville, MD 20857.

II. General Discussion

The skin, as the protective covering of the body, is frequently subjected to injuries. Microorganisms, both resident and transient, dwell on the surface of the skin, and when the skin is broken, there is always the possibility that harmful microorganisms might spread from the site of injury to the deeper tissues or into the bloodsteam, producing a serious infection.

The Panel believes that decreasing the number of microorganisms on the surface of the skin is rational OTC therapy when the skin surface has been broken by a minor cut or scrape, prior to breaking the skin for removal of a splinter, or prior to injection. Ethyl and isopropyl alcohol possess many desirable features as antimicrobial agents in such therapy. The antimicrobial effectiveness of ethyl and isopropyl alcohol is not impressive against fungi and viruses. However, these alcohols are bactericidal; that is, they kill bacteria instead of preventing their growth and immobilizing them, which would be a bacteriostatic action. In addition, these alcohols evaporate readily and remove dirt and grime. Because ethyl and isopropyl alcohols are colorless, they do not stain the skin and thus would not mask inflammation, a warning sign of infection.

The Panel does not recommend that a consumer attempt to use an alcohol to self-treat a deep, extensive wound, or a puncture wound, or attempt to remove a large or deeply embedded splinter. Professional treatment should be sought immediately for such injuries. Alcohols are not recommended in these instances, as they have an irritant effect on damaged, deeply cut tissue (Ref. 1). The irritant action of alcohols is particularly marked on mucosa. The more concentrated the alcohol, the more pronounced are its irritant effects (Ref. 2). The Panel recommends caution in the use of topical alcohols on the mucous membranes in concentrations recommended for antimicrobial use in this document.

References

(1) Zanowiak, P., "Topical Anti-Infective Products," *in* "Handbook of Nonprescription Drugs," 16th Ed., American Pharmaceutical Association, Washington, p. 371, 1979.

(2) Ritchie, J. M., "The Aliphatic Alcohols," *in* "The Pharmacological basis of Therapeutics," 5th Ed., edited by L. S. Goodman and A. Gilman, The MacMillan Co., New York, pp. 137–146, 1975.

III. Categorization of Data

A. Category I Conditions

These are conditions under which alcohol active ingredients for topical antimicrobial use are generally recognized as safe and effective and are not misbranded.

1. *Category I ingredients.*

Ethyl alcohol
Isopropyl alcohol

a. *Ethyl alcohol.* Ethyl alcohol (ethanol) has been used in beverages for centuries, and its medicinal, pharmacological, and nutritional properties have been studied extensively. Alcohol is an established name for ethyl alcohol (Ref. 1); however, the Panel will refer to the ingredient as ethyl alcohol in this document in order to distinguish clearly between it and isopropyl alcohol. Ethyl alcohol has an astringent action, precipitating protein; it cools the skin surface by rapid evaporation and, therefore, has been used topically to lower the body temperature; it produces mild redness and a burning sensation when rubbed on the skin and can be used as a counterirritant and rubefacient; and it cleans the skin by its solvent action on oils and greases.

Because of its solvent action, ethyl alcohol is also frequently used in a diluted form as a vehicle for other topical medications. It is capable of altering the stratum corneum (skin surface) and enhancing its permeability, thus facilitating the penetration through the skin of any ingredient that is dissolved in it (Ref. 2). This has been demonstrated with corticosteroids (Ref. 3), salicylic acid (Ref. 4), and iodine (Ref. 5).

Ethyl alcohol rubs have been used in hospitals for many years, and ethyl alcohol is also used frequently on bedridden patients as an adjunct to prevent decubitus ulcers (bedsores) (Ref. 6). However, washing the skin with a 74-percent concentration of ethyl alcohol has been reported to result in the recovery of increased numbers of surface inoculated *Staphylococcus aureus* 5 hours later. The assumption was that an increase in bacteria occurred as a result of removing antibacterial organic matter through the defatting action of the alcohol (Ref. 7).

Ethyl alcohol that is marketed for topical OTC use contains denaturants which are added to make it unsuitable for drinking purposes.

(1) *Safety.* The long use of ethyl alcohol in beverages attests to its relative nontoxicity when ingested in small quantities. It is readily absorbed from the stomach, small intestine, and colon, and vapors may be absorbed from the lungs. After absorption, ethyl alcohol is fairly uniformly distributed through the tissues and fluids of the body, and 90 to 98 percent is slowly and completely oxidized (Ref. 6).

Regardless of how ethyl alcohol enters the body, its greatest effect is on the central nervous system, and it acts as a primary and continuous depressant (Ref. 6). A concentration of 50 milligrams (mg) ethyl alcohol per 100 milliliters (mL) blood may impair muscular coordination and judgment, and a concentration of 200 mg per 100 mL of blood may produce a state of mild-to-moderate intoxication. A concentration of 300 mg per 100 mL blood will cause severe alcoholic intoxication, and a fatal concentration is estimated to be about 400 mg per 100 mL blood (Ref. 6).

Contact allergy to the lower primary aliphatic alcohols (methyl, ethyl, and propyl) has been reported, but is rare (Refs. 8 and 9). Because ethyl alcohol has been reported to be 7.5 times more toxic to white blood cells in vitro than to staphylococci (Ref. 10), its use is not recommended for open, extensive wounds. The application of antimicrobial concentrations of ethyl alcohol to such wounds might possibly do more harm than good by interfering with the body's basic defense mechanisms. The Panel therefore limits its recommendation for OTC use of this ingredient to application to minor cuts and scraps, application to the skin prior to breaking it for the removal of small splinters that are not deeply embedded, and for preparation of the skim prior to an injection.

(2) *Effectiveness.* Ethyl alcohol has been shown by in vitro and in vivo tests in kill bacteria. Some interesting early work on the antibacterial effectiveness of ethyl alcohol was conducted by Prombo and Tilden (Ref. 11) and Nungester and Kempf (Ref. 12). The most plausible explanation for this action is the denaturing of proteins by this ingredient. The most concentrated form of ethyl alcohol (100 percent), however, is less bactericidal than mixtures of ethyl alcohol and water. (See tables below.) This is probably because proteins are not denatured so readily in the absence of water as when water is present (Ref. 13).