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Abstract

In recent years there has been increasing use of antibacterial agents employed in toilet bars to provide deodorant and degerming activity. The common desirable properties of these agents are antibacterial activity at low concentrations, skin substantivity, acceptable color and odor, compatibility with the vehicle, and low irritation and sensitization potential.

Bacteriostats used for such purposes are principally bisphenolics, halogenated salicylanilides, and halogenated carbanilides. Methods for assessing their effectiveness and safety are discussed. The polybrominated salicylanilides represent a versatile group of bacteriostats which enjoys increasing acceptability in toilet bars and also provides benefits in such household products as liquid detergents, granulated detergents, hardsurface disinfectant cleansers, and aerosol disinfectant sprays.

Introduction

IN THE PAST TWO DECADES soap and detergent products have seen revolutionary changes in composition to provide a multiple array of actions. From the simple old-fashioned goal of all cleansing agents, that of ridding surfaces of soil, there are now literally hundreds of different cleansing formulations—bars, liquid detergents, granulated detergents, and tablets all formulated not only to provide cleaning action but also to offer ancillary benefits. A multitude of additives are employed in household products to provide suds boosting, whitening and brightening, hand care and mildness, sanitizing, disinfecting, bleaching, detergent building, fabric softening, and deodorizing.

For the toilet bars, additives in use provide such actions as degerming, inhibition of odor development, skin softening, complexion care, scum-dispersing action, and nonalkaline washing.

Antibacterial Agents

Of all the adjuncts in use, the one class that has had the greatest impact in recent years on the consumer market for soaps and detergents has been the antibacterial agents. Some representative agents in toilet bars and household laundry products are given in Table I. They are divided into several classes. The simple phenolics, like *o*-benzyl-*p*-chlorophenol, find their chief use in disinfectant-cleanser products and disinfectant sprays where the action desired is killon-contact as defined by the United States Dept. of Agriculture. Such products must satisfy the AOAC Use-Dilution Test requirements, viz., kill of *S. aureus* and *S. choleraesuis* in 10 minutes under strictly prescribed testing conditions (1).

The simple phenolics are limited in use to the area of hard-surface disinfection. They do not possess the properties of significant residual action or substantivity to fabrics or skin. The polybrominated salicylanilides have proved quite versatile since they enhance the activity of phenolic formulations by providing a long-lasting action in addition to the quick kill required for disinfectants (2). Also formulations containing the polybrominated salicylanilides are substantive to fabric and are useful as sanitizing agents when added to the laundry wash cycle either with the detergent or in the final rinse (3).

Three important classes of antibacterial agents employed in toilet bars today are the bisphenolics, polybrominated salicylanilides, and the halogenated carbanilides. These germicides in toilet bars have the following desirable properties in common: effectiveness against Gram-positive skin bacteria (micrococci) at low concentrations (These bacteria are the principal residents of skin and are not inhibited by plain soap washing.); an affinity for skin such that, during washing, the germicide is adsorbed on the epidermis and is not washed off during the rinse operation (The presence of trace amounts of the germicide remaining on the skin has the effect of suppressing the growth of the skin micrococci that feed on the skin secretions and detritus. Thus the typical "body odor" resulting from bacterial attack is effectively suppressed.); compatibility with soap and nonsoap "actives"; stability to light and heat; activity in the presence of soil (Soil includes blood and skin secretions.); and very low skin-irritation potential.

Screening Methods

There is no dearth of published data on methods for assessing the activity of these soap bacteriostats. They are screened essentially the same way in most laboratories.

The Toxic Dilution Test is first run to determine whether the agent is effective, preferably at about 1-2 ppm or less in a nutrient medium. The influence of vehicle or soil can be studied in such a system. The affinity of the bacteriostat is checked in some substantivity test, such as the Skin Disc Substantivity or Finger Imprint Tests (4).

The degerming efficiency of a soap containing an effective bacteriostat is determined in a panel of subjects given the test bar to use regularly for one or two weeks. Before and after the test period the subjects' hands are washed with plain soap in a series of basins in accordance with some modification of the Price Serial Basin Wash Test. The percentage reduction in bacterial counts is calculated by relating the bacterial counts of wash water after the test period to the initial counts as a baseline. This value represents the degerming efficiency of the test bar. An effective soap will give percentage degerming of skin varying from 60 to more than 90% (5).

The deodorant properties of a soap are best assessed in an under-arm odor test. One realistic method in this laboratory is to select a panel of male subjects demonstrated to have axillae of high odor-intensity. These subjects are washed under one under-arm with the test soap and under the other under-arm with the control soap. The following day the axillae are rated for odor intensity on a blind-basis, and washes are repeated. Sniff ratings are taken the next day; then

		TABLE	5 1				
Representative	Antibacterial La	Agents undry P	in 'rod	Toilet ucts	Bars	and	Household

Agents	Chemical Name	Chief Use Sanitizer or disinfectant in acrosols and hard-surface liquid cleansers		
Simple phenolics	o-Phenyl phenol o-Benzyl-p-chlorophenol Tertiary amyl phenol			
Bisphenolics	Hexachlorophene Bithionol	Soap bacteriostat, laundry bacteriostat, sanitizer		
Halogenated salicylanilides	3.4',5-Tribromosalicylanilide (tribromsalan) alone or in combination with 4',5-dibromo- salicylanilide (dibromsalan)	Soap bacteriostat, laundry bacteriostat Sanitizer and disinfectant Bacteriostat in liquid detergents		
Halogenated carbanilides	3,4,4'-Trichlorocarbanilide 3-Trifluoromethyl 4,4'-dichlorocarbanilide	Soap bacteriostat, laundry bacteriostat Soap bacteriostat		
Miscellaneous	Quaternary ammonium compounds Iodophors	Sanitizer or disinfectant Laundry bacteriostat Sanitizer or disinfectant for aerosol and hard-surface liquid cleansers		

a third and final washing is made. After time intervals of 24, 48, and 72 hours, sniff ratings are made again on the axillae and T-shirts worn for this study. Data indicate that an effective degerming soap (60%)or better in reducing hand bacterial counts) will have an inhibitory effect on under-arm odor that will last up to 72 hours after the final washing. Little or no differences can be detected between deodorant soaps on the market. All of them are effective in this test.

Deodorant soaps on the market today contain from 0.5 to 2.0% of germicides. There is a recent trend to employ multiple systems of germicides; binary and ternary mixtures are common. This has the effect of increasing the germicidal potency of mixtures which can be demonstrated in laboratory screening and Serial Basin Wash tests.

Safety of Soap Bacteriostats

Assessing topical agents like soap bacteriostats for mildness under use-conditions is not a difficult problem if the proper toxicological procedure is applied on animals, followed by human testing to screen out primary irritants and sensitizers. This does not mean that acceptable agents may not provoke occasional reactions in hypersensitive subjects, which may, in the large population, occur one in 10,000 or one in 100,000 subjects. Complete exclusion of all potential sensitizers of the marginal type is literally impossible to establish in laboratory and clinical trials. For example, even if there were no adverse effects in 30,000 persons tested, one in 10,000 (0.01%) would be still liable to skin reaction.

In the past two years, reports have come out in the dermatological literature that implicate soap bacteriostats in isolated cases of photodermatitis. Jillson and Baughman first reported several cases of subjects designated as persistent light-reactors reacting to bithionol (6). They were observed to be crosssensitized to some halogenated salicylanilides and even to hexachlorophene. Other investigators like Epstein (7), Mollov and Mayer (8), and recently Harber and Baer (9) have reported additional cases of subjects photosensitized to one or more halogenated salicylanilides. The need to report such findings is unquestioned since physicians should be alerted in dealing with cases of photodermatitis in hypersensitive patients. Thus they can be in a better position to diagnose and suggest treatment.

Unfortunately these reports of rare instances of photodermatitis which have been linked to deodorant soaps have, on occasion, been misinterpreted and so distorted as to imply that the problem is more widespread than a handful of hypersensitive subjects in literally millions of consumers.

One of the reasons for the recent adverse publicity on 3,4',5-tribromosalicylanilide (tribromsalan), alone or in combination with 4',5-dibromosalicylanilide (dibromsalan), stems from the reports of photodermatitis caused by soaps containing tetrachlorosalicylanilide (TCSA). No question exists regarding the photosensitizing potential of TCSA, and it was so reported about five years ago in England by Wilkinson (10) and in the United States by Vinson and Flatt (11). Unlike TCSA, tribromsalan and a mixture of dibromsalan and tribromsalan have a very low photosensitizing potential as determined in animal and human studies.

The safety and acceptability of soaps containing polybrominated salicylanilides are attested to by the following. Tribromsalan and dibromsalan have been employed in soaps for more than nine years; literally hundreds of millions of bars have been sold, and the consumer acceptability has been excellent. Experimental studies on guinea pigs have shown that tribromsalan alone¹ and in combination with dibromsalan² have no photosensitizing action under exaggerated testing conditions in use today (12). Data soon to be published, employing the exaggerated Draize-Shelanski and Schwartz-Peck tests made even more abusive by exposing the subjects to UV-irradiation, indicate that soap containing tribromsalan alone or in combination with dibromsalan is without photosensitizing action (13).

¹ Temasept II, Fine Organics Inc. ² Temasept I, Fine Organics Inc.

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