ON THE MODE OF ACTION OF SELENIUM SULFIDE*

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Although selenium sulfide shampoo (Selsun®) is widely used in the treatment of dandruff and seborrhea, the mode of action of selenium sulfide is unknown. The literature on this subject is contradictory. The fact has been stressed that locally applied selenium sulfide in Selsun has no toxic effect. In support of this assumption it has been pointed out that after use of the shampoo the urinary selenium levels were in the normal range (1). This argument does not carry much weight, because in well-established cases of selenium poisoning the urinary selenium levels were often normal (2, 3). It has been also claimed that the action of selenium was related to that of sulfur on account of its proximity to this element in the periodic table (1, 4). However, the pharmacologic actions of selenium resemble more closely those of arsenic (5). Finally, the possibility has been also suggested that the effect of selenium sulfide was essentially due to the sulfur released from this combination (6).

One definitely established fact about selenium compounds in general is their ability to inactivate free sulfhydryl groups and compounds through mercaptide formation, in the same way as arsenic. This sulfhydryl inactivating effect has been demonstrated in vitro with sulfhydryl compounds (7) and enzymes (8, 9), and in vivo by protecting animals poisoned with selenium salts by the administration of glutathione (10) or BAL (11). In order to test whether or not selenium sulfide had a similar sulfhydryl inhibitory effect as other selenium salts, various tissues were incubated with selenium sulfide suspensions and their sulfhydryl content determined.

EXPERIMENTAL

The following tissues were used for in vitro studies: 1. Powdered epidermal keratin from scales of a patient with psoriatic exfoliative dermatitis. 2. Ten per cent aqueous mouse liver homogenates. 3. Ten per cent aqueous homogenates of human epidermis, separated with the stretch method (12). The selenium sulfide suspensions and the controls employed were as follows: 1. Selsun® (2.5% selenium disulfide shampoo) and a Selsun placebo† which presumably had the same composition as Selsun, except for a lower selenium sulfide content (0.1%), both diluted 5 times with water. 2. Two per cent Duponol C (sodium lauryl sulfate) with 0.5% selenium disulfide suspended and 2% Duponol as control. 3. An aqueous suspension of selenium disulfide with water as control. Incubation ranged from 10 to 60 minutes and was carried out at room temperature, 40°C and (in the case of keratin) in a boiling water bath. Sulfhydryl was determined with Bennett’s reagent (13).

RESULTS

There was a significant and consistent inhibition of free sulfhydryl groups when mouse liver and human epidermis were incubated with the selenium disulfide-detergent suspensions (Table I).

No consistent effect on epidermal keratin was found.

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DISCUSSION

These experiments bring proof that selenium sulfide has a definite chemical action. The finding that under our experimental conditions Selsun had relatively little inhibitory effect on the sulfhydryl groups of human epidermis does not necessarily mean that this shampoo is relatively inert, because the placebo which served as its control also contained selenium sulfide, although in a 25 times smaller concentration. The actual concentrations, however, give no information about the amounts of ionized (active) selenium in solution. Therefore, the truly significant experiment is the one in which Duponol, containing selenium sulfide, was compared with Duponol itself. In this experiment it was conclusively shown that selenium sulfide inactivated the sulfhydryl groups of human epidermal homogenates under experimental conditions (10 minutes at 40°C) similar to those encountered during the actual therapeutic use of Selsun Shampoo.

The combination of a detergent with a sulfhydryl inhibitor gives rise to an interesting chain of reactions. Detergents, as recently shown by Van Scott and Lyon, increase the amount of reactive sulfhydryl groups in epidermal keratins, presumably by exposing formerly masked sulfhydryl groups (14). By such a process of denaturation, detergents similarly affect other proteins (15), including those of the epidermis (16). Thus the effect of a selenium sulfide shampoo is twofold: on the one hand, the detergent releases previously non-reactive sulfhydryl groups and the selenium compounds then inactivate some of these groups.

On the basis of the present study, it is not permissible to speculate whether or not this double action is responsible for the therapeutic effect of Selsun. It is of interest to point out that selenium-containing waters have been used by Napoleon for the treatment of "diseases of keratinization" among his troops (17). Disorganized and inhibited processes of keratinization are also prominent symptoms of selenium poisoning in cattle (7, 17, 18).

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<th>TABLE I</th>
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<td><strong>Inactivation of free sulfhydryl with selenium sulfide-detergent suspensions</strong></td>
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<td>TISSUE</td>
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<td>Mouse liver (10 mg)</td>
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<td>Selsun 5X diluted (0.5 ml)</td>
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<td>Human epidermis (10 mg)</td>
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Selenium disulfide in vitro inactivates the free sulfhydryl groups of human epidermis and mouse liver. The effect of Selsun shampoo is twofold: due to its detergent action it makes available previously non-reactive sulfhydryl groups, some of which then are inactivated by selenium disulfide.

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