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Major article

# Dermal and pulmonary absorption of propan-1-ol and propan-2-ol from hand rubs

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***Background:*** It has been shown that nontoxic concentrations of ethanol are absorbed after hand hygiene using ethanol-based hand rubs. This study investigated whether absorption of propan-1-ol and propan-2-ol from commercially available hand rubs results in measurable concentrations after use.

***Methods:*** The pulmonary and dermal absorption of propanol during hand rubs was investigated. Rubs contained 70% (w/w) propan-1-ol, 63.14% (w/w) propan-2-ol, or 45% (w/w) propan-2-ol in combination with 30% (w/w) propan-1-ol.

***Results:*** Peak median blood levels were 9.15 mg/L for propan-1-ol and 5.3 mg/L for propan-2-ol after hygienic hand rubs and 18.0 mg/L and 10.0 mg/L, respectively, after surgical hand rubs. Under actual surgical conditions, the highest median blood levels were 4.08 mg/L for propan-1-ol and 2.56 mg/L for propan-2-ol. The same procedure performed with prevention of pulmonary exposure through the use of a gas-tight mask resulted in peak median blood levels of 1.16 mg/L of propan-1-ol and 1.74 mg/L of propan-2-ol.

***Conclusion:*** Only minimal amounts of propanols are absorbed through the use of hand rubs. Based on our experimental data, the risk of chronic systemic toxic effects caused by hand rubs is likely negligible. However, our study did not evaluate the consequences of long-term daily and frequent use of hygienic hand rubs.



Given that hands are the primary vehicle for transmission of microbial pathogens causing infections, hand hygiene is essential for infection control in any health care setting,[1-10] as well as in the community.[11-13] Most alcohol-based hand rubs contain ethanol, propan-1-ol or propan-2-ol, or a combination of these alcohols.[1,2,10] In previous studies of hand rubs with ethanol-based formulations, under extreme test conditions usually not encountered in the health care setting, 0.5%-2.3% of the applied ethanol was absorbed, resulting in blood levels of <30 mg/L (0.023%). Although absorption was found, in practice the use of ethanol-based hand rubs is considered safe.[14,15]

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Comparable blood levels were found for propan-2-ol; in a study using a commercial hand rub applied every 10 minutes over a 4-hour period, subjects' blood levels of propan-2-ol ranged from 0.5 to 1.8 mg/L.[16] Leeper et al[17] reported that after extensive epidermal application of 273 g of propan-2-ol, only 0.9% was absorbed within 10 hours. In contrast, Brown et al[18] found negligible blood levels of propan-2-ol in subjects who applied a hygienic hand rub 30 times in a 1-hour period. Propanol-2-ol also was not detec\table in the breath of these subjects. However, the Brown et al study used a method that is approximately 30-fold less sensitive than the method used in the study of Turner et al[16] and in the present study.

The dermal and inhalation absorption of propan-2-ol is supported by case reports on intoxication.[19-22] After preoperative skin antisepsis in pediatric surgery, serum levels of up to 12.2 mg/L (mean, 5.0 $\pm$ 3.37 mg/L) were documented by Wittmann et al.[23]

Compared with propan-2-ol, the data on absorption of propan-1-ol is even scantier. On isolated human epidermis, the following constants of permeability have been determined: 800 cm/hour for ethanol, 1,200 cm/hour for propan-1-ol, and 1,350 cm/hour for propan-2-ol.[24,25] Peschel et al[26] demonstrated that after modified surgical hand rubs with propanol-containing products with and without the ingestion of alcoholic beverages, propan-2-ol and propan-1-ol levels could disturb the analysis of congeners. Measured propan-1-ol levels were generally 0.2-1.8 mg/L, with levels pf 8.8 mg/L and 14 mg/L measured in 2 subjects.

The aim of the present experimental study was to determine the absorbed amounts of propan-2-ol and propan-1-ol from the use of commercially available hand rubs. The primary goal is to assess the toxicological risk from the absorption data. We tested 3 hand rubs containing propan-1-ol alone, propan-2-ol alone, and both in combination under the same worst-case conditions as in our previous study examining ethanol absorption,[14] as well as under clinical conditions with and without pulmonary exposure.

## METHODS

### *Study design and setting*

All 3 experiments had a controlled blinded design and were approved by the Ethics Committee of the Board of Physicians of Mecklenburg-Pomerania, University of Greifswald (BB 07/09). In experiment 1, under a worst-case model of excessive hygienic or surgical hand rubs, hand rub application was performed in a 37 $m^3$ room with 2 open windows and an open door, without controlled air exchange during applications. Between hand rub applications, participants were placed in a second room in which the use of alcohol-based hand rubs was not permitted. Blood samples were collected in another separate room.

Experiment 2 involved surgical hand rubs, including a hygienic hand rub on entering the surgical theatre. Absorption was determined during the routine surgical program, which included 3 interventions of approximately 90 minutes each. Blood samples were collected in the doctors' lounge in the surgical suite.

Experiment 3 was performed in the same manner as in experiment 2, but pulmonary exposure was prevented through the use of a gas-tight mask (X-plore 4390 with A2 filter; Draeger, Lübeck, Germany) during hand rub application and while the surgeon was in the wash room.

### *Participants*

Twelve participants (6 males, 6 females) participated in experiment 1, 10 surgeons (6 males, 4 females) participated in experiment 2, and 10 participants (6 males, 4 females) participated in experiment 3. For all experiments, inclusion criteria were age at least 18 years and the ability to perform a standardized application according to European Standard EN 1500:1997.[27] Exclusion criteria were defined as visible skin lesions on hands or arms, skin disease, alimentary intake of ethanol, and use of cosmetics in any form within 24 hours before the start of a test and on the day of the test. Furthermore, individuals with diabetes mellitus, pregnant or lactating women, and individuals who participated in a clinical experiment within 30 days before the start of the study also were excluded. To exclude potential oral alcohol consumption by participants, we also determined the ethanol levels of all participants during the 3 experiments. Written consent was obtained from all participants.

### *Hand rubs*

Three commercially available hand rubs were tested: hand rub P1 (Skinman Sensitive, 70% w/w propan-1-ol; Ecolab, Düsseldorf, Germany), hand rub P2 (Manorapid ready for use, 63.14% w/w propan-2-ol; Antiseptica, Pulheim, Germany), and hand rub P1P2 (Sterillium Classic Pure, 45% w/w propan-2-ol in combination with 30% w/w propan-1-ol and 0.2% w/w mecetronium etilsulfate; Bode Chemie, Hamburg, Germany). All hand rubs were applied in both hygienic and surgical hand rubs. The hand rubs did not contain any fragrance or dye but a mixture of skin care components.

### *Hand rub application*

In experiment 1, both hygienic hand rubs and surgical hand rubs were performed with P1P2 and P2, because at the time that this experiment was conducted, a hand rub containing only propan-1-ol was not commercially available. Hands were washed with nonmedicated neutral soap and dried thoroughly immediately before the start of the experiment. For each hygienic hand rub, 4 mL of hand rub was applied in the test room to both hands and rubbed in for 30 seconds according to the standard rub-in procedure described in EN 1500:1997.[27] After waiting for 1 minute outside the test room, this procedure was repeated. A total of 20 hygienic hand rubs were performed, resulting in a total exposure time of 10 minutes over a 30-minute period.

The surgical hand rub experiments were started 7 days after the hygienic hand rub experiments. Here, 4 mL of hand rub was applied to the hands and rubbed on the hands and forearms. This procedure was repeated 5 times, with the hands and forearms kept covered with the hand rub for the recommended application time of 3 minutes.[28] After a 5-minute wait outside the test room, the procedure was repeated. A total of 10 surgical hand rubs were performed, resulting in a total exposure time of 30 minutes over an 80-minute period. For hygienic and surgical hand rubs, each hand rub was tested individually on one of 2 consecutive test days. At the end of each test day, a skin care cream (Neutrogena; Johnson & Johnson, Düsseldorf, Germany) was applied to the treated skin areas.

For experiments 2 and 3, when entering the surgical theater, a hygienic hand rub was performed. This hygienic hand rub was performed for 30 seconds with the same hand rub as used for the surgical hand rub. Then, 10 minutes later, a surgical hand rub with an application time of 1.5 minutes was performed before each of 3 consecutive 90-minute surgical interventions. The exact volume of the product applied for both the hygienic hand rub and the 3 surgical hand rubs was noted and used to calculate the absorption rate. After the hand rub application and air-drying, surgical gloves and gowns were donned.