

## Hand Sanitation and the COVID-19 Pandemic

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The present COVID19 pandemic has raised the alarm across the globe. While we are rapidly learning how its genetic makeup differ from other corona strains (1–3), we are still without effective prophylactic or therapeutic drugs against the disease. The public Health care systems are doing their utmost to prevent a spread of the disease by demanding that citizens wash or disinfect their hands multiple times every day in order to prevent transfer of COVID19 from hands to the mouth, nose or eyes (1). The underlying assumption is that the washing process or the exposure to disinfectant is sufficient to eradicate or reduce sufficiently the viral load on the hands (4, 5). Here we will focus our discussion on the soap-based hand washing process, and the associated problems with skin irritation caused by the choice of soap as well as other active molecules in the soap mixture.

Various types of natural materials have served as soaps throughout history. A common aim has been to remove dirt from the hair, skin or clothing. This often implied that lipid or lipophilic compounds needed to be removed. But these compounds do not dissolve readily in water. Ash mixed with water was probably one of the earliest materials that was used to remove lipidic compounds. Ash makes the water more alkaline – thus the pH may increase to 9. At this pH many fats start to hydrolyse into their constituent components, a fatty acid and an alcohol. During this process the remaining fat becomes negatively charged from the free fatty acids that dissolve in the hydrophobic fat. This electrostatic charge will increase the likelihood for solubilization. A fraction of the released fatty acid may partially dissolve in water and formation of micron-sized fatty acid containing micellar aggregates can accompany this process.

Water has a very high surface tension due to the adhesion of one water molecule to other water molecules in its molecular neighbourhood. If a water droplet rests on a hydrophobic surface it forms a near spherical shape where the curvature of the droplet

is a measure of the surface tension. This inherent self-adhesion prevents water from entering into fabrics where the fibres form a tight mesh. However, if one adds amphiphilic molecules, i.e. molecules that are both hydrophobic and hydrophilic, to the water that lowers the water's tendency to self-adhesion and the water will be able to penetrate into the fibre mesh and detach the dirt. A fatty acid with a charged functional group in one end and a long aliphatic chain in the other end.

The skin naturally exhibits a pH around 4.5–5.8 through the secretion of acidic compounds (termed the Acid Mantle). In addition, the skin secretes a cocktail of hydrolytic enzymes. Because it is acidic, the most effective way to clean this, together with excessive oils, dirt and microorganisms, is to use an alkaline-foaming soap. The soap will separate this acid-mantle from the skin. Within 20 min it is back on one third of its original power, and within 2–3 h it is completely recovered.

It is becoming evident that the human skin hosts a rich collection of microorganisms, ranging from bacteria to fungi and virus (6). They are found in the upper layer of epidermis and in hair follicles. Most of these organisms are commensal, some are symbiotic and very few are pathogenic. The normal skin maintains its slightly acidic pH in part due to bacterial secretions of hydrolytic enzymes, that are presumed to combat pathogenic bacteria. Whenever we wash our hands this protective layer is removed, but is re-established within hours of the washing process. During the recovery period, it is reasonable to assume that the skin is susceptible to pathogenic microorganisms.

Modern soaps consist of an amphiphilic organic chain with a functional group at the terminal. Sodium lauryl sulfate (SLS) has been a preferred standard soap. However, soaps based on SLS have pH values between 7.5 and 9. The alkaline pH may cause irritation of the skin, but a range of other factors also play a role. The top layer of protective lipids that cover healthy skin will be dissolved by repeated exposure to soaps. Thus,

repeated handwash in a clinical setting may result in skin irritation (atopic dermatitis) with possible microbial infection of the unprotected and damaged skin. Interestingly, it has recently been reported that 20% of COVID-19 patients developed rashes or chickenpox-like blisters on the torso. Microbial infection can occur through damaged skin. Normally, this involves primarily bacteria, for example staphylococcus, and not viruses. Currently, we assume that COVID-19 cannot be transmitted through damaged skin and wounds, but is transmitted via mucous membranes.

The anti-viral effect of the soap is presumed to be caused by the soap dissolving the lipid membrane of the virus particle, but currently very little concrete evidence concerning the COVID-19 virus in particular is available. What we do know is that handwashing with soap in general is more anti-viral than is hand rub with an ethanol or alcohol based disinfectant (4, 5). It is also known that different type of soaps have different effects on the anti-viral potential of the soap (9). The human influenza virus was very efficiently removed using a potassium oleate (C18:1) soap – whereas sodium laureth sulfate (LES) and sodium lauryl sulfate (C12:0) (SLS) were 1,000 times less efficient on the same virus. It is known that other fatty acids as well as monoglycerides show similar anti-viral effects to potassium oleate. Monolaurin is reported to disintegrate envelope virus.

LES and SLS are common in standard household soaps. Thus, the anti-viral effect must be a combination of both a physical chemical pH-related effect and a specific biochemical effect of the particular soap that is used. The biochemical effect is likely to be virus-dependent as well. We propose that the affinity of the free fatty acid for insertion into the viral double membrane is a critical parameter, and the degree of saturation as well as chain length is likely to be important. It is known that specific fatty acids like arachidonic acid (AA) and other unsaturated fatty acids (especially eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA)) can inhibit enveloped virus. It is plausible that the COVID-19 exploits the human hosts array of fatty acids and cholesterol for synthesizing copies of its own lipid membrane envelope.

One of the major comorbidities of COVID-19 is obesity. Obesity is associated with a high systemic level of cholesterol. Cholesterol is known to modify the dynamics of the mammalian cell membrane. In a recent Chinese study of COVID-19 patients the serum levels of cholesterol were found to be significantly lower than normal. Does COVID-19 recruit the patients' cholesterol for constructing its lipidic envelope? The influence and possible functionally modulating role of cholesterol and other lipidic compounds on COVID-19 is therefore an interesting topic and relevant for formulating optimized

hand washing soaps. Very recently a study has appeared that documents a statistically significant correlation between low vitamin D levels and COVID-19 mortality, especially in the elderly. One may wonder if the observed enhanced COVID-19 mortality for the Afro-American population in the US is linked to vitamin-D deficiencies?

In conclusion, there is no doubt that hand sanitation is crucial for controlling the COVID-19 epidemic. Though few details are known about the COVID-19 virus' physical biochemistry we have here presented literary evidence that soap-based handwashing is superior to hand rubbing with alcohol fluids or gels. The choice of soap molecule is also important and we recommend to use potassium oleate or another potent fatty acid or mono-glyceride and not to use SLS. Other anti-viral actives may be added to the soap. Care should be given that actives or soaps do not prevent the natural skin microbiome to re-populate the skin. In order to prevent skin irritation due to repeated hand washing we recommend to re-establish the lipid protection layer on the skin using cosmetic creams for extra dry skin.

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