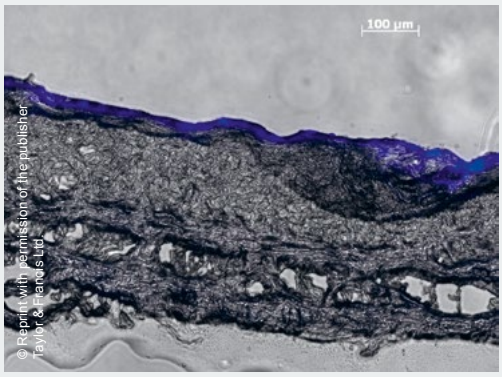
Permeable protective barrier

Which substances get through the skin in what amounts? Experiments at the BfR simulate how potentially health-damaging substances penetrate our largest contact organ.



Substances permeate the skin

Microscopic image of a section of human skin after contact with the material of a hammer handle containing polycyclic aromatic hydrocarbons (PAHs).

Substances can make their way into the body through many different pathways. The three most important ones are the digestive tract, the lungs and the skin. Uptake via the skin is a domain that has hardly been explored up to now with regard to risk assessment. Methods are being sought by means of which the dermal absorption of substances can be realistically estimated.

Toxic hammer grip

In 2009, headlines such as "Poison in hammer handles" and "Poison from the one euro shop" gave the public quite a scare. High levels of polycyclic aromatic hydrocarbons (PAHs) had been detected in numerous consumer products made of elastic polymeric materials, such as bike handlebar grips, gardening shoes and the shafts of many tools. Several of these, such as benzo[a]pyrene (B[a]P), are carcinogenic. As long as these substances remain in the material, they do not pose a risk to health, but what happens when people work with the tools or wear the rubber shoes all day long?

There were no science-based answers to these questions, as there was a lack of examinations and suitable tests. In a research project, the BfR developed a method with which quantities of B[a]P that are transferred from the elastic material of a hammer handle to the skin can be realistically examined upon skin contact. This approach could also clarify whether, just like other substances, B[a]P also penetrates into the deeper layers of the upper skin (epidermis) and the corium (dermis) that lies below.

Experiments with Franz cells

Tests with Franz cells were the starting point. The principle of this test is that a material sample lies directly on a piece of animal or human skin. The skin acts as a membrane with the epidermis tending upwards and the dermal side in contact with a receptor liquid (see chart on page 34). A test run usually takes several hours. "This method is the gold standard in examinations of dermal absorption," says project leader Dr. Christoph Hutzler. It is commonly applied in the testing of cosmetics and pharmaceutical substances. The method has hardly been relevant up to now in toxicological tests of materials. "We were able to show, however, that apart from friction or pressure, the Franz cell test imitates migration in real skin contact with hammer handles fairly well."

Experiments were conducted with material samples from various hammer handles and a toy tyre containing known quantities of B[a]P. Epidermis from human donor skin was used as a membrane in order to establish the most realistic exposure scenario. Pig's epidermis, artificial human epidermis cultivated in a laboratory and a synthetic membrane were used for comparison purposes. Food chemist Dr. Nastasia Bartsch conducted the experiments. After 24 hours, during which the system was kept at 33 degrees Celsius, she determined the quantities of B[a]P which entered the skin. Result: 102 nanograms B[a]P were present in one square centimetre of human skin caused by skin contact with a hammer handle containing 166 milligrams of B[a]P per kilogram material. During the process, four fifths of the migrated B[a]P remained in the outermost layer of the epidermis, the stratum corneum, and one fifth permeated to the deeper layers. Some of it even diffused into the receptor liquid.

In conclusion, B[a]P overcame the protective barrier of the epidermis and reached the dermis below that is crisscrossed with fine blood vessels. Consequently, it was concluded, the substance can also find its way into the blood circulation via these blood vessels.

A look through a fluorescence microscope revealed the permeation pathway. A blue fluorescence signal that is typical of PAHs can be seen in the images of wafer-thin skin samples from the Franz cell. This means that PAHs accumulate in the stratum corneum after contact with the hammer grip and diffuse further from this reservoir into the deeper skin layers.

New substances targeted

What happens on a cellular basis upon skin contact with B[a]P containing materials? This question was recently addressed in experiments using molecular biological methods. B[a]P from the hammer handle damages the genetic material in the nucleus of intact skin cells. This finding is of concern, because it can contribute to the development of skin cancer. For this reason, Germany succeeded on EU level in ensuring that limit values have now been set to restrict the occurrence of this potentially health-damaging substance in consumer products made of rubber or plastic. In the meantime, the team headed by Christoph Hutzler has expanded the examination method to include other critical substances present in plastics. A close eye is being kept here on various plastic additives, such as plasticisers, antioxidants and their breakdown products, which occur through the ageing of the material. The first results show that these can also overcome the outer skin barrier and permeate to the deeper skin layers to varying extents. ◘

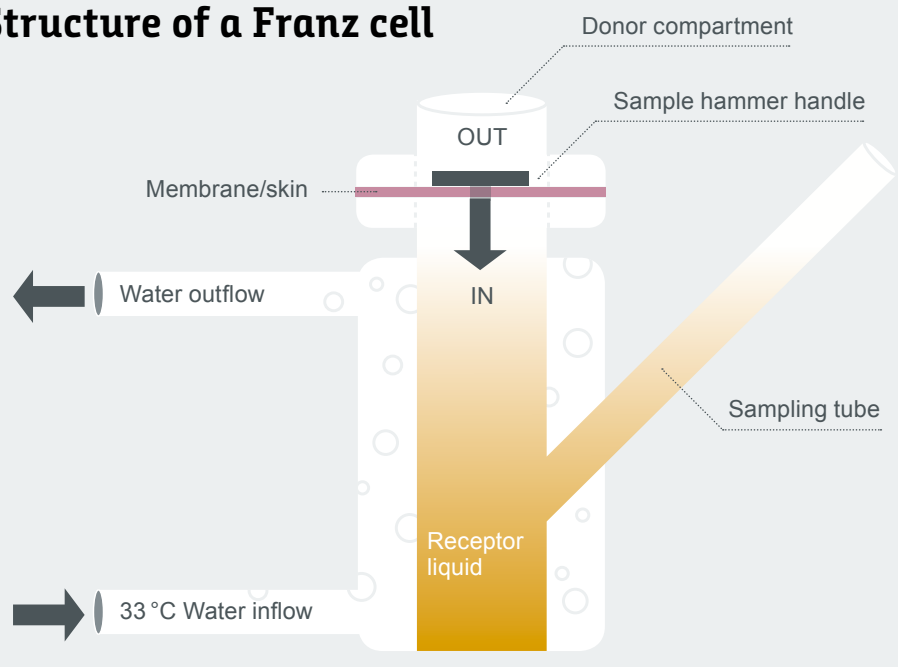
Prediction model suitable for routine use

Examinations with Franz cells are elaborate and not suited as routine tests, so is there an easier way to establish exposure values? Sweat simulant testing, which is otherwise the method commonly used for materials with skin contact, dramatically underestimates dermal exposure. If the aqueous simulant contains 20% ethanol, as shown by experiments conducted by the BfR, the material gives off the same quantity of B[a]P into the simulant compared to the human skin exposure in the Franz cell test. This prediction model developed by the BfR has been tested on national and European level and used as an examination method in the national monitoring programme. It is suitable for estimating the health risk of materials containing PAHs which have contact with the skin.

More information:
Bartsch et al. 2016. Skin permeation of polycyclic aromatic hydrocarbons: A solvent-based in vitro approach to assess dermal exposures against benzo[a]pyrene and dibenzopyrenes. J Occup Environ Hyg 13(12): 969–979. doi: 10.1080/15459624.2016.1200724

Dissertation paper: Nastasia Bartsch. 2019. Polymer additives, contaminants and non-intentionally added substances in consumer products: Combined migration, permeation and toxicity analyses in skin. https://refubium.fu-berlin.de > dissertations FU

Structure of a Franz cell



The cell consists of a double-wall vessel filled with receptor liquid and with a donor compartment on top. Heated water flows between the two walls of the vessel in a water jacket. A membrane or skin sample with full contact with the receptor liquid is stretched between the vessel and the donor compartment.