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Hygienic Relevance and Risk Assessment of Antimicrobial-Impregnated Textiles

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Abstract

The antimicrobial impregnation of textiles is intended to provide protection of textiles against microbial corrosion, prevention of malodor or prophylaxis and therapy of infections, respectively. For every biocidal product a careful risk assessment for humans and the environment has to be performed. The advantage of antimicrobially active textiles has to be documented for every agent as well as for every application, and a balance has to be found between a textile's quality rating and the potential risks, e.g. sensitization, disturbance of the ecology of the skin, toxic side effects by means of systemic absorption, cytotoxicity, genotoxicity, carcinogenicity, teratogenicity and ecotoxicity. This article evaluates the applicability of silver compounds as well as the classic antimicrobials triclosan, quaternary ammonium compounds, copper and further new options like chitosan and zeolite. It has to be emphasized that there are no objections against the use of antimicrobially active textiles if their use is equal or superior to other preventive or therapeutic measures. This applies to the amelioration of the course of dermatological diseases with disturbed skin flora, in particular atopic dermatitis, the prevention and therapy of acute and chronic wound infections by wound dressings, the use of impregnated surgical suture material as well as special indications in the prevention of infection in medical facilities. The use of antimicrobial textiles for the prevention of dermatomycosis by antifungal impregnation is of questionable use; the antimicrobial impregnation of textiles for deodorization purposes has to be avoided. Presently, from a hygienic point of view, the following questions have to be clearly determined: declaration of any antimicrobial impregnation; development of international standards for in vitro testing and preclinical evaluation of efficacy and tolerance; evaluation of the advantage of the antimicrobial properties for the intended use including the risk-benefit assessment.

Herbs and spices for the conservation of textiles, e.g. for embalming mummies, were already used by the pharaohs [Vigo, 1983]. During the

Second World War, the German army used uniforms impregnated with quaternary ammonium compounds (quats) under the suggestion that secondary wound infections can be prevented [Arnold, 1963]. At the same time Engel and Gump [1941] recommended hexachlorophene impregnation of cotton and wool.

With the worldwide expansion of synthetic textiles the need for antimicrobial impregnation of textiles increased substantially as synthetic textiles absorb about 25% less water vapor compared to cotton or wool. The blocking of evaporation of sweat results in a thin fluid film on the skin, which consequently impairs further the evaporation of sweat, providing an ideal environment for proliferation of bacteria and fungi. Soon, commercial interest was directed to the antimicrobial impregnation of natural fibers.

Purpose and Risks of Antimicrobial-Impregnated Textiles

The purpose of antimicrobial impregnation of textiles is:

- elimination of malodor by deodorization or absorption;
- increasing the lifetime of technical textiles, but also of household textiles and leather by prevention of microbial corrosion (e.g. moulding, discoloration);

an official assessment of 109 textile and leather samples disclosed biocidal concentrations between 1 and 649 mg/kg in 77 samples, thereof 4-chlor-3-cresol up to 200 mg/kg, 2-phenylphenol up to 210 mg/kg and 2-(thiocyanatomethylthio) benzothiazole up to 540 mg/kg in leather clothing, and pentachlorphenol(!), 4-chlor-3-cresol and 2-phenylphenol up to 2 mg/kg and triclosan up to 640 mg/kg in textiles (www.bfr.bund.de, 11th session of the working group 'health assessment of textile adjuvants and dyes');

- prevention of dermatomycosis by antifungal impregnation;
- impact on the progress of dermatological diseases by alteration of skin flora;
- prevention or therapy of wound infections;
- prevention of infections in medical facilities.

Regarding the side effects for humans and the environment, every textile with antimicrobial activity must undergo a risk assessment. At the same time, also the benefits derived from the use of the biocide have to be assessed and balanced for its risks.

The following side effects can be provoked by biocides:

- sensitization and manifestation of allergic disorders, in particular as contact eczema;

- anaphylactic reaction (presently described only for chlorhexidine [Kramer, 2001]);
- negative impact on the microecology of the skin with influence on colonization resistance (presently not evaluated in detail);
- induction of development of antimicrobial resistance including cross-resistance with antibiotics;
- with long-term application dermal absorption of biocides and dose-related chronic toxicity including genotoxicity, cancerogenicity and teratogenicity have to be investigated;
- in case of missing or low-degree biological degradation, of high-level burden or toxification of biocides, the cumulative ecotoxic effects have to be assessed.

In Germany the actual federal regulation of textile declaration requires only information about the textile fibers but not about the adjuvants. However, according to the food and legislation act for articles of daily use (§ 30), the manufacture of articles of daily use with potential health hazards is restricted. Up to now this has required neither declaration nor obligatory registration. The presently used practice to declare biocides only in case of allergic potential is not satisfactory. Regarding the risk potential a general declaration is required. In future, biocides for impregnation of textiles can only be used, when they are contained in the 'positive list' of the biocide product guideline.

Hygiene Assessment for the Use of Antimicrobial-Impregnated Textiles

Deodorants

Besides local dermal applications impregnated textiles or synthetic fleece are rarely used for deodorization [Untiedt, 2004]. The intended use for textiles impregnated with a deodorant is to prevent bacterial degradation of sweat not at the site of the skin but in the textile itself. The impregnation of textiles for deodorization is inevitably less active than the direct application of the deodorant to the skin, as the contact of an antimicrobial-impregnated textile with the skin, e.g. in the axilla, is substantially worse. Therefore this application cannot legitimately be recommended. Regarding the environmental burden, the application at the site of the textile has to be considered as more critical than the dermal application.

The use of antibacterial textiles for infants and children is controversial. In the light of the hypothesis that infections in early childhood may be protective against the development of allergic disorders [Strachan, 1989; Cookson and Moffatt, 1997; Matricardi, 1997; Matricardi and Bonini, 2000; Matricardi et al., 2000; Friedrich et al., 2006], reduction of the skin flora might be hazardous [Bodner et al., 1998; Farooqi and Hopkin, 1998; Bager et al., 2002; Gibbs et al., 2004].

A potential explanation provides the Th1/Th2 paradigm [Mosmann et al., 1989; Romagnani, 1992]. The two helper cell subsets Th1 and Th2 are characterized by different patterns of cytokine production and have different functions. Th2-derived cytokines inhibit the development of Th1 cells and vice versa. Atopic diseases are Th2 mediated and characterized by the release of IgE, whereas bacterial and viral infection are more likely to be Th1 mediated. Thus, the infection-induced Th1-cell-specific cytokine inhibits the development of allergen-specific Th2 cells. This theory is however not uniformly accepted.

The endowment of towels with deodorizing agents is principally contradictory. This is also valable for the addition of deodorants into the wash process for laundry and rugs.

Conclusion: Dirty and smelling textiles must be cleaned with detergents. It does not make sense to block and to override the smell by deodorants.

Protection against Mouldiness and Bacterial Destruction

The antimicrobial impregnation of textiles improves durability. Antimicrobial textiles can be used for tents, covers, curtains, nets, sacks, technical felts, filters and special work clothes [Wallhäusser and Fischer, 1970]. The choice of the appropriate antimicrobial agents must follow strict toxicological and ecological criteria. The necessity must be carefully evaluated.

Antifungal Impregnation

Modern clothing materials provide an optimal milieu for growth of bacteria and fungi, because synthetic fibers create a moist chamber with maceration of the skin [Meyer-Rohn and Kulenkamp, 1975]. As synthetic fibers cannot be boiled, fungi and bacteria can survive and cause colonization, infection or reinfection, respectively. Shoes play a crucial role in the development of plantar mycosis. In a study with several thousands of soldiers, it was found that wearing sandals resulted in 3.5% plantar mycosis in contrast to 28% of persons wearing closed shoes [Taplin, 1976]. In common public facilities [Salminen et al., 1974; Kraus and Tiefenbrunner, 1975] as well as in pedicure salons, shoe shops and locker rooms, fungal spread takes place, which cannot be controlled by the use of antifungal textiles. This can predominantly be achieved by personal hygienic measures, wearing comfortable well-aerated shoes, avoidance of barefoot walking in risk zones and antimycotic therapy in early stages of infection. In public facilities with high risks for dermatomycosis, basic preventive measures by the employer are mandatory. Carefully drying the feet including the space between the toes together with skin care is important [Seebacher and Kramer, 1997].

Conclusion: There is neither an epidemiological nor a hypothetic justification for antifungal endowment of textiles for the prevention of fungal infections.

It is rather sufficient to change textiles regularly, to wash or clean underwear and socks at a minimum of 60°C. If this is not possible, the laundry of persons with overt dermatomycosis as well as of particularly predisposed persons can be washed at 30°C, yet the addition of disinfectant cleaner is helpful.

Adjuvant Therapy of Dermatomycoses

In contrast to the previous opinion that an allergic pathogenesis is exclusively responsible for the typical lesions seen in patients with atopic dermatitis, recent research results suggest a 2-step pathogenesis. It is still commonly accepted that the initial trigger is an allergic antigen-antibody (IgE) reaction. However, newer studies found that bacteria and fungi are responsible for the maintenance of clinical symptoms, for the exacerbations and progression of the disease. The skin, altered by the inflammatory process, is colonized by substantially higher amounts of bacteria. Therefore modern therapeutic strategies focus on the adjuvant antimicrobial therapy of atopic dermatitis.

An early start of therapy with antimicrobial active immune modulators, e.g. tacrolimus and pimecrolimus, which are thought to modify the allergic part of the disease, can prevent the outbreak and the spread of eczematous skin lesions. In addition to the immunomodulatory effect, these medications are antimicrobially active as the basic molecule of these compounds is a macrolide antibiotic.

A good clinical efficacy has been demonstrated with silver-coated antimicrobially active textiles without evidence of bacterial resistance. It has been documented that the antiseptic activity of silver-coated textiles can reduce the colonization with *Staphylococcus aureus* as well as the production of staphylococcal exotoxin whereby the inflammatory reaction is suppressed [Werfel, 2001]. In contrast to impregnation of textiles with silver salts, metallic silver exhibits a good tissue tolerance. Starting with an enteral absorption of >2 g of silver, argyrosis has been observed, which is a deposition of silver in the superficial skin layers. The amount of silver, which is absorbed even through damaged skin by the inflammatory process, is 1,000-fold below the toxic level even when the textile is used over years.

The cumulative costs of therapy are limited to the initial costs of the silver-coated textile.

Nevertheless the declaration of silver impregnation cannot be correlated with clinical efficacy. Three different textiles endowed with silver by different technologies (No. 1: 50% of fibers are coated with metallic silver, No. 2: 50% polyamide fibers with a durable silver staining, No. 3: silver-impregnated Trevira) have been investigated for their antimicrobial activity.

Pieces of 1 cm^2 of the textiles were incubated with a suspension of 10^9 colony-forming units (CFU) of the test organism. In 3-hourly intervals, 50 μl of

Table 1. Number of surviving bacteria after exposure to three silver textiles (No. 1–3) for various reaction times

Textile No.	Test organism	Bacterial count, log CFU						
		3 h	6 h	9 h	12 h	15 h	18 h	24 h
1	*S. aureus*	9	8	6	4	0	0	0
	S. epidermidis	8	6	4	0	0	0	0
	E. coli	6	4	0	0	0	0	0
	P. aeruginosa	8	7	6	5	0	0	0
2	*S. aureus*	9	8	6	5	0	0	0
	S. epidermidis	8	6	0	0	0	0	0
	E. coli	6	4	0	0	0	0	0
	P. aeruginosa	8	7	5	0	0	0	0
3	*S. aureus*	9	9	8	8	7	7	7
	S. epidermidis	9	8	8	7	6	6	6
	E. coli	9	8	7	7	7	6	5
	P. aeruginosa	9	8	8	8	7	7	6

The value 0 means below the level of detection of 10^5 CFU/ml.

the suspension were inoculated on Columbia agar (containing 50% sheep blood). After incubation for 24 h the number of CFU was determined.

Table 1 shows substantial differences between the different silver textiles [Guggenbichler, unpubl.].

In another study the influence of a moisture-permeable silver textile on the skin of 5 healthy volunteers was investigated.

An area of 10 × 10 cm was tightly covered with one of the samples manufactured according to the technologies described above . Every 3 h for the first 9 h and 6 h thereafter the number of CFU on 1 cm^2 of skin was determined.

At the beginning of the experiment, a mixed flora consisting of *Staphylococcus epidermidis, Propionibacterium acnes* and *Streptococcus mitis* in an amount of 4.3–5.5 log CFU/cm^2 was isolated. Textiles No. 1 and 2 reduced the skin flora every 3 h by 1 log, so that at 9 h no organisms could be isolated any more. This effect lasted for another 9 h; thereafter, the normal flora gradually recolonized the skin so that at 36 h the normal skin flora in the amount mentioned before could be detected. No irritation of the skin occurred during the experiment. Textile No. 3 did not show any antibacterial effect. Twenty-four-hour extracts of these three textiles in physiological saline were investigated for cytotoxicity on mouse fibroblasts. No reduction of viability was seen with the methylene blue test with any of the textiles [Guggenbichler, unpubl.].

Table 2. Mean total number ± SD of isolated microorganisms in neurodermitic skin lesions (log CFU/cm^2) of patients (determination by direct agar contact method)

Group	Day 0	Day 14	Day 28	p[1]	Day 56	p[2]	p[3]
Ag textile	1.87 ± 0.51	1.41 ± 0.82	1.35 ± 0.64	0.07	1.45 ± 0.46	0.6	0.03
Cotton	1.59 ± 0.88	1.41 ± 0.97	1.42 ± 0.67	0.6	1.53 ± 0.95	0.9	0.9

[1]t test with paired samples, comparison between day 0 and day 28.
[2]Comparison between day 28 and day 56.
[3]Comparison between day 0 and day 56.

In a controlled clinical trial with patients suffering from atopic dermatitis, the influence of silver underwear on the normal skin flora was investigated over a period of 1 month. Patients in the first group were wearing silver textiles manufactured according to technology No. 1 (see above) throughout from day 0 to day 28. The patients in a second group were wearing identical cotton underwear without silver from day 0 to day 14 and then the silver textile from day 14 to day 28. From day 28 all patients returned to their individual underwear. In the first group bacterial reduction on the skin with neurodermitic lesions over a period of 56 days was observed. In the group with the patients wearing silver textiles for 14 days, no significant reduction of the skin flora was noted (table 2). Apparently wearing this silver underwear for 14 days is not sufficient for a substantial reduction of the skin flora. The analysis of microorganisms revealed an analogous reduction for *S. aureus* and *S. epidermidis*. The lower number of colonizing organisms which was observed on day 56 warrants additional attention as it is assumed to be a remanent effect. It is conceivable that silver deposits in the skin could be responsible for this reduction. In order to obtain further insight into this hypothesis, silver elimination in the urine was investigated. In the urine no silver was detected (threshold of detection 0.9 μg/ml).

Clinical evaluation of the patients revealed that silver underwear worn over the longer period resulted in a significant improvement of the SCORAD (Scoring Atopic Dermatitis) index compared to the group with a shorter wearing period. The silver underwear does not tolerate washing temperatures above 60°C. Therefore the overall hygienic impression was unsatisfactory. After wearing the textiles for more than 2 days, the patients were disturbed by malodor and discomfort, which increased with duration of use [Jünger et al., 2006].

Other groups of investigators achieved comparable results. In an open controlled trial with 15 patients, two sites of neurodermitic lesions in the same

patients were compared over 14 days. The elbow of one arm of the patients with neurodermitis was covered for 7 days with a silver-coated material, the other site with normal cotton. Thereafter an observation period of 7 days followed. After 2 days a significant reduction of colonization with *S. aureus* was observed on the site covered with the silver textile. The total number of CFU of skin flora remained below the initial concentrations of skin microorganisms on the control site for another 7 days. The SCORAD at the beginning of the experiment was identical on both arms. On days 2, 7 and 14 the SCORAD was substantially improved on the silver-textile-covered arm. During the follow-up period, the difference between the silver textile and the control site was still accentuated. In 5 patients the condition remained stable; in another 6 patients further improvement was observed. At the site covered by cotton without silver, a slight but nonsignificant clinical improvement of the eczematous lesion was observed on day 2. On days 7 and 14 the SCORAD deteriorated. The comparison between the two sites revealed an optical improvement with the silver textile ($p < 0.05$) on days 7 and 14 [Gauger et al., 2003].

In a randomized, controlled clinical trial with atopic dermatitis patients (35 patients with silver-coated textiles, 22 with placebo), an improvement of the SCORAD – in the silver group of 27.4% ($p < 0.05$) and in the placebo group of 16.3% ($p > 0.05$) – was observed. The affected area of the skin in the silver group regressed by 16.6% ($p < 0.05$) and by 8.3% ($p > 0.05$) in the control group; the difference versus placebo was at the threshold of significance ($p = 0.051$). An equal improvement was seen in the DIELH score (Deutsches Instrument zur Erfassung der Lebensqualität bei Hauterkrankungen; score of Schäfer et al. [2001]). After 7 days, the patients noted a recognizable improvement in itching, comfort and dryness in the silver versus the placebo group ($p < 0.05$). The differences became accentuated after 14 days. Also, concomitant medication (corticosteroid ointments) was more frequent in the placebo group ($p > 0.05$) [Schäfer, in prep.].

Conclusion: An improvement in the therapy of atopic dermatitis by silver-coated/impregnated textiles could be demonstrated and must be confirmed in larger studies, before being advised as therapeutical option.

Prevention of Postoperative Wound Infections

The impregnation of suture material is a promising approach to the prophylaxis of postoperative wound infections.

After surgical interventions in microbially colonized areas, the risk of wound dehiscence is given. Interventions in areas colonized with $<10^5$ CFU/g tissue normally are without risk for postoperative wound infections in immunocompetent hosts [Elek and Conen, 1957]. However, with impaired host defense mechanisms, foreign bodies and ischemia, even substantially lower amounts of microorganisms ($<10^3$ CFU) are

able to cause a wound infection [Schmitt, 1991]. In the presence of suture material even concentrations of 10^2 *S. aureus*/g tissue are critical [Elek and Conen, 1957]. Sutures in abdominal surgery are generally pulled through the lumen of the gut and are contaminated with a variety of aerobic and anaerobic bacteria. Under these circumstances a wound infection and dehiscence of the suture must be taken into consideration. Clinical experience shows that sutures in the large intestine are more frequently insufficient than sutures in the stomach. The proportion by which sutures are responsible for a primary wound infection can only be resolved by clinical studies comparing the incidence of postoperative wound infections in patients with antimicrobial sutures and in controls. Vincent [2003] reports an incidence of postoperative wound infections of 15%. The risk of implanted foreign bodies, e.g. sutures or clips as primary cause for nosocomial wound infections, is estimated to be low; however, implanted biomaterials play a major role in the perpetuation of infections; the percentage is unknown (no studies).

In vitro studies demonstrate a zone of inhibition for *S. epidermidis* around a triclosan-impregnated suture of 14.5 cm^3, for *S. aureus* or methicillin-resistant *S. aureus* (MRSA) of 17.8 cm^3. The antibacterial activity lasted 7 days [Rothenburger et al., 2002]. However, a disadvantage of triclosan-impregnated sutures is the intrinsic resistance of triclosan against *Pseudomonas aeruginosa, Serratia marcescens* and *Alcaligenes* spp. In vivo studies confirmed the efficacy.

Sutures were implanted in the dorsolateral thighs of guinea pigs; 5×10^4 CFU *S. aureus* were instilled into the wound by a catheter, and 48 h later the suture was explanted. Thereafter $10^{3.6}$ CFU were isolated from nonantimicrobially active suture material in contrast to $10^{1.85}$ CFU in triclosan-impregnated sutures ($p < 0.05$) [Storch et al., 2002a, 2004]. The addition of triclosan to the suture did not influence physical properties and the handling of the device [Storch et al., 2002b].

No cytotoxic effect of the impregnated sutures was observed in tissue cultures, and the material was nonpyrogenic. No intracutaneous and intramuscular side effects were observed. Between the triclosan-impregnated materials and nonimpregnated materials, in none of the animal models differences could be detected [Barbolt, 2002]. Accordingly any difference in the healing process of experimental wounds in guinea pigs could be disclosed [Storch et al., 2002a].

Conclusion: The use of antimicrobial-impregnated surgical suture materials is beneficial, particularly in critically contaminated wounds and in patients with a high risk of infection. The benefit for reduction of postoperative wound infections has to be documented in clinical trials. The uptake of triclosan with a suture is toxicologically noncritical. As long as the in vitro inducible development of resistance to triclosan has no clinical relevance, the use in suture material is uncritical [Kramer et al., 2005a]. A promising alternative approach will be the use of nanocristalline silver.

Table 3. IC_{50} of antiseptic agents on mouse fibroblasts after 30 min of exposure [Müller and Kramer, unpubl.]

Agent	IC_{50}, mg/ml
Ag[1]	0.007–0.055
Silver sulfadiazine	0.030–0.040
Polyhexanide	0.150–0.200
Povidone-iodine	4.7–4.8

[1]Results of Poon and Burd [2004], calculated on the basis of silver.

Antiseptic Wound Dressings

For the prevention of postoperative and posttraumatic wound infections as well as for the treatment of acute wound infections, antisepsis (irrigation, ointment, gel) in combination with surgical debridement is the method of choice [Kramer et al., 2004]. For colonized or infected chronic wounds, it is important to eliminate the microorganisms and toxins without disturbing the wound-healing process. For this purpose antiseptic wound dressings with simultaneous absorption of toxins are useful [Müller et al., 2003]. Presently silver-containing wound dressings represent the state of the art. Wound dressings which do not release silver into the tissues are preferable especially to prevent disturbance of the healing process.

The toxic effect of Ag^+ is caused by the interaction of silver ions with the cell membrane and the respiratory chain (reaction with cytochromes b and d and the substrates of oxidation [Weber and Rutala, 2001]) of newly formed epithelial cells. In keratinocyte and fibroblast cell cultures, $AgNO_3$ and nanocristalline silver are highly toxic in concentrations of 7×10^{-4} to 55×10^{-4}% [Poon and Burd, 2004]. In comparison povidone-iodine and polyhexanide show substantially less cytotoxicity (table 3).

Hidalgo et al. [1998] investigated the therapeutic activity (MIC/cytotoxicity) of silver nitrate. Depending on microorganisms, growth inhibition was detected after 100- to 700-fold dilution with even measurable cytotoxicity. As a consequence 0.01% was recommended as therapeutic concentration. Innes et al. [2001] compared the time for reepithelialization in a mesh graft model (prospective controlled matched-pair study). The criterion of >90% reepithelialization ($p = 0.004$) was seen in a silver-free dressing environment after 9.1 ± 1.6 days, in a silver-containing dressing after 14.5 ± 6.7 days. There was no difference in bacteriological culture positivity. After 1 and 2 months, scar formation was significantly worse by use of a silver-containing dressing compared

to a silver-free dressing. After 3 months the initial differences evened out. In addition the risk of systemic side effects by liberation of free silver ions has to be taken into consideration. After the application of silver sulfadiazine on burn wounds, silver concentrations of 440 μg Ag/l blood and 12 μg Ag/l urine were found [Maitre et al., 2002]. The authors recommend the monitoring of silver levels, when silver-releasing compounds are used.

In order to estimate the relevance of the in vitro cytotoxicity, we evaluated the minimal microbicidal concentration (MMC, defined as reduction factor ≥5 log steps) in 10% fetal calf serum in a quantitative suspension test. Silver sulfadiazine was ineffective. 1% $AgNO_3$ reduced the inoculum size of *Escherichia coli* by maximally 1 log. Within 30 min all silver-containing compounds were inactive against *S. aureus*. Against *E. coli* the concentration of >5% of mild silver protein solution was active. For the comparison of antiseptics we introduced a biocompatibility index as quotient of IC_{50} and MMC ≥5 log. For $AgNO_3$ and silver sulfadiazine no biocompatibility index could be calculated, because the highest tolerated concentration (1%) did not result in any reduction of the initial inoculum size. Colloidal silver resulted in a biocompatibility index (L929-cells/*E. coli*) of 0.128, chlorhexidine had one of 0.729, povidone-iodine (related to iodine) one of 0.95, polyhexanide one of 1.325 and octenidine one of 1.506. Silver-containing antiseptics are highly cytotoxic without measurable antimicrobial activity within 30 min [Müller et al., 2006]. However, after 3 h of exposure of a wound dressing, a reduction of 5 log steps against *P. aeruginosa* ATCC 15442 was noticed [Müller et al., 2003]. These data indicate that a slow release of low silver ion concentrations is effective after an extended period of time. The induction of silver resistance cannot be excluded in case of prolonged and low-level release of silver ions [Percival et al., 2005].

Conclusion: Colonized or infected chronic wounds require the application of adequate antiseptic wound dressings with the ability of toxin absorption, e.g. endotoxins. When silver-containing wound dressings are used, the liberation of silver into the wound environment should not reach cytotoxic concentrations. The antimicrobial activity of silver in dressings cannot be compared with the rapid bactericidal action achieved by other antiseptics. Over a period of several hours, low nontoxic concentrations of silver ions are antiseptically effective and block the attachment of microorganisms to epithelial cells as well as biofilm formation. The activity of silver in dressings depends on the technology of silver bonding.

Prevention of Infections in Medical Facilities

No evidence exists for any preventive effect of antimicrobial-impregnated bedlinens, diapers, work clothes and towels. If basic hygienic measures are taken (e.g. hand disinfection, disinfection of patients near surfaces, change of textiles at regular intervals, barrier nursing) the antimicrobial equipment of

textiles cannot provide additional protective effects. The skin as reservoir of microorganisms remains active as a source of bacterial spread; nevertheless, the amount of bacteria can be reduced. In addition the risk of sensitization has to be taken into consideration. In contrast, the antimicrobial endowment of air filters can be sensible, if no active compounds are liberated into the environment. Equally the antimicrobial endowment of lacquers, e.g. for door knobs or siphons, of flexible partition walls and of textile linings is meaningful and allows the avoidance of prophylactic disinfection. For this purpose nanocristalline silver seems to be the agent of choice.

The disinfection of surfaces or skin antisepsis by means of fleeces impregnated with biocide must be considered as a special case of application of antibacterial textiles.

In Germany the solution for fleeces is listed in the positive list of the German Confederation of Applied Hygiene, if the recommended antimicrobial activity of the solution is fulfilled. This does not apply to antimicrobial-impregnated disinfecting fleece and requires a comment insofar as the impregnated fleece does not achieve the activity of the active solution per se. One textile, impregnated with 70% propan-2-ol, is effective and registered as drug for skin antisepsis in Germany.

Conclusion: For special indications antimicrobial-impregnated textiles can provide a valuable contribution to the prevention of infection.

Methods of Antimicrobial Impregnation of Textiles and Hygienic Consequences

Highly diffusible impregnations are differentiated from nondiffusible or poorly diffusible antimicrobial impregnations. For impregnation, the Foulard application is most often used, where the active compound is applied during the spinning process. Further techniques for application of antimicrobial substances are coating, vapor deposition (e.g. silver), spray application, aftertreatment in a bath (e.g. for triclosan) or treatment of prefabricated items in a washing machine, which is ecotoxicologically questionable. Even when liberation into the environment is excluded, the ecological safety of the applied biocide with respect to waste disposal must be considered. Besides, the impossibility of liberation of the active agent must de documented not only for the ready-to-use product, but also during usage, because sweat, antimicrobial degradation and/or the washing process can lead to hazardous secondary products. It has been documented that triclosan can be transformed into the toxic 2,7/2,8-dibenzodichloro-*p*-dioxin by sunlight in sewage; this can be detected in sewage plants [Mezcua et al., 2004].

Characteristics of Selected Compounds for the Antimicrobial Impregnation of Textiles

Taking triclosan as an example, the problems of antimicrobial impregnation of textiles will be demonstrated. Other compounds are described briefly.

Triclosan (2,4,4'-Trichloro-2'-Hydroxydiphenylether)

Antimicrobial Activity and Spectrum of Activity

Within 10 min of exposure, the MMC measured for *S. aureus* and *Candida albicans* was 25 μg/ml, for *E. coli* 500 μg/ml. Within 72 h the MMC for *S. aureus* was 0.1 μg/ml, for *E. coli, Proteus* spp. and *Klebsiella pneumoniae* 0.03–0.3 μg/ml, for *Enterobacter aerogenes* 1–3 μg/ml, for *Enterococcus faecalis, C. albicans* and *Saccharomyces cerevisiae* 3–10 μg/ml [Räuchle, 1987; Wallhäusser, 1995]. *P. aeruginosa* shows a high intrinsic resistance with an MIC of >1,000 μg/ml [Räuchle, 1987; Chuanchuen et al., 2003]. Triclosan inhibits the growth of *Pityriasis versicolor* at a concentration of 75 μg/ml within 1–2 days almost completely but does not eradicate the organism [Hundt et al., 2000].

The mode of action consists in the inhibition of the enoyl-acyl carrier protein reductase [McMurry et al., 1998, 1999; Levy et al., 1999; Heath and Rock, 2000], which destabilizes the membrane. The fatty acid synthase system (type II) of bacteria is substantially different from the mammalian enzyme, which can be an option for selective inhibition [Marrakchi et al., 2002].

Development of Resistance

Exposure of microorganisms to subbactericidal concentrations in vitro can induce resistance [Hundt et al., 2000; Hundt, 2001; Brenwald and Fraise, 2003]. Cookson et al. [1991] described strains of MRSA with MICs between 2 and 4 μg/ml from patients with daily triclosan total body washings, whereas *S. aureus* strains from patients without exposure to triclosan exhibited MICs between 0.01 and 0.1 μg/ml. As a result of the specific point of attack of triclosan on the bacterial cell, the enoyl-acyl carrier protein reductase [Heath and Rock, 2000], and because the resistance development mechanisms against antibiotics are comparable to that against triclosan (target mutation, increased target expression, active efflux from the cell, enzymatic deactivation/degradation), laboratory findings related to the cross-resistance between triclosan and antibiotics are not surprising [Russell et al., 1998; Chuanchuen et al., 2001, 2002, 2003; Braoudaki and Hilton, 2004, 2005; Randall et al., 2004; Sanchez et al., 2005].

The genetic product of *fab*I, the enoyl-acyl carrier protein reductase, evolved as a major target site for the development of resistance to triclosan [McMurry et al., 1999]. *E. coli* strains with mutation of the *fab*I gene frequently showed low, medium or high triclosan resistance (MICs between 0.2 and

25 μg/ml [McMurry et al. 1998]). *S. aureus fab*I mutants also showed increasing MICs (1–4 μg/ml) against triclosan [Brenwald and Fraise, 2003]. *Mycobacterium smegmatis* strains with a mutation of the *inh*A gene are resistant to triclosan as well as to isoniazid. It has been suggested that also the tuberculostatic activity of isoniazid is based on *inh*A products [Levy, 2001]. The discussion whether plasmid-coded antibiotic resistance is able to induce triclosan resistance is still controversial. Although it has been shown by Cookson et al. [1991] that triclosan resistance against *S. aureus* can be transferred simultaneously with the plasmid-coded mupirocin resistance, this could not be verified by other investigators [Suller and Russell, 2000].

On the basis of these laboratory findings it would be conceivable that, as result of the widespread use of triclosan particularly in consumer products [Furuichi et al., 1999; Braid and Wale, 2002] antibiotic resistances could be selected [Schweizer, 2001], although up to now no organism with acquired triclosan resistance has been described [Gilbert and McBain, 2002; Screenivasan and Gaffar, 2002; De Vizio and Davies, 2004]. Also the MIC values have remained stable during the last decade [Goodfellow et al., 2003]. No clinical data exist regarding a triclosan-induced resistance against antibiotics [Suller and Russell, 1999; Russell, 2000, 2002, 2003]. The clinical relevance of the previous laboratory findings has to be elucidated [Suller and Russell, 2000]. Until this point the use of triclosan should be limited to medically proven indications.

Acute Toxicity

On the basis of LD_{50} (mg/kg body weight, BW), determined by oral application, to mice of 4,500, to rats of 3,700–5,000, to dogs of 5,000 and, by dermal application, to rabbits of 9,300 [Räuchle, 1987], the compound is classified as 'little to nontoxic'. The subcutaneous LD_{50} for rats is $>$147,000 mg/kg BW [De Salva et al., 1989], which suggests the categorization 'nontoxic'.

In the rat, no changes of glutamic oxaloacetic transaminase, glutamic pyruvic transaminase and blood urea nitrogen were observed after a single oral dose of 625 and 2,500 mg triclosan/kg BW in contrast to chlorhexidine after oral administration of $\geq$1,000 mg/kg BW. In vitro, a dose-related inhibition of the accumulation of *p*-aminohippurate but not of N-methylnicotinamide in the kidney of male rats was observed. The clinical relevance of these laboratory findings has to be established [Chow et al., 1977].

Skin Tolerance and Photosensitization

The antiseptic concentration for use was tolerated without adverse effects. A good skin tolerance has even been established in the 'repeated-insult patch test' with soaps containing 10% triclosan [Räuchle, 1987]. Trials with humans did not reveal any phototoxic reactions [Kligman and Breit, 1968].

Eye Tolerance

Solutions of 1–10% induced a transient hyperemia and chemosis which resolved after 24 h [Räuchle, 1987].

Sensitization and Photosensitization

Photosensitization was demonstrated neither in animal experiments nor in clinical studies [Marzulli and Maibach, 1973; Thomann and Maurer, 1975; Räuchle, 1987; Wnorowski, 1994]. Although occasionally photosensitization has been described, the widespread use of triclosan in deodorants and soaps apparently indicates an exceedingly low potential for sensitization [Roed-Petersen et al., 1975; Lachapelle and Tennstedt, 1979; Hindson, 1975; Wahlberg, 1976; Veronesi et al., 1986; Steinkjer and Braathen, 1988; Wong and Beck, 2001; Gloor et al., 2002]. However, 10 from 88 patients with (photo)allergies to UV filters in suncreams reacted to triclosan [Schauder, 2001]. In a second investigation among 103 patients, 3 responded with an allergic contact reaction and none with a photoallergic reaction [Steinkjer and Braathen, 1988]. Two of these patients received ointments containing corticosteroid and 3% triclosan. A Swedish investigation showed a prevalence of 0.2% (1,100 patients investigated) of contact allergy to triclosan [Wahlberg, 1976].

Subacute Toxicity

The subacute toxicity test (28 days) in monkeys revealed a no observable effect level (NOEL) of 100 mg/kg BW/day [Räuchle, 1987]; the daily administration of 0.1% triclosan solution over 3 weeks to dogs revealed no signs of toxicity [Schmid et al., 1994].

Subchronic Toxicity

In a subchronic toxicity test (90 days of oral administration for various animal species), the NOEL (mg/kg BW/day) reached for hamsters was 75, for rats 50, monkeys 30, dogs 12.5 and rabbits 3 [Paterson, 1969; Goldsmith, 1983; Räuchle, 1987; Schmid et al., 1994]. With dermal application of 3% triclosan in propylene glycol to rabbits, no local or toxic reaction was observed [Räuchle, 1987].

Chronic Toxicity and Cancerogenicity

For monkeys the NOEL was 30 mg/kg BW after oral administration over 1 year [Drake, 1975]. In a 2-year test in rats, 250 and 750 mg/kg in nutrition were well tolerated. After administration of 2,200 mg/kg, a mild reversible liver hypertrophy developed [Räuchle, 1987].

The inducible hepatotoxicity after administration of high doses of triclosan is obviously due to a competitive and noncompetitive inhibition of the 3-methylcholanthrene- and phenobarbital-inducible P450-dependent monooxygenase in liver microsomes by triclosan [Hanioka et al., 1996].

A feeding test over 2 years revealed no signs of cancerogenicity at a doses of 168 mg/kg/day in male rats or 218 mg/kg/day in female rats [Yau and Green, 1986; Räuchle, 1987]. The serum concentrations of triclosan in this test were between 26 and 27 mg/l. An independent review of this study reaches the same conclusion [Goodman, 1990]. Also in hamsters the harmlessness was documented [Chambers, 1999]. A dermal application of 0.5 and 1% triclosan in acetone over 18 months was well tolerated, and no signs of cancerogenicity occurred [Räuchle, 1987].

Mutagenesis and Reproduction Toxicity

Neither in vitro nor animal experiments revealed any signs of mutagenesis, embryotoxicity or teratogenic effects [Russell and Montgomery, 1980; Gocke et al., 1981; Räuchle, 1987; Henderson et al., 1988a, b; Jones and Wilson, 1988; Morseth, 1988; Riach et al., 1988; Denning et al., 1992; Schroder and Daly, 1992].

Absorption and Elimination

In experiments with rats, rabbits and dogs no organospecific accumulation of triclosan was detected. The elimination occurs after conjugation with glucuronic acid in the feces, in rabbits mainly renally. In humans the renal elimination as glucuronic acid or as sulfate conjugate represents the main route. The half-life counts 10 days without signs of cumulation [Räuchle, 1987; Cantox, 2002]. Through intact skin, 10–25% of the administered dose is absorbed [Black et al., 1975].

Ecotoxicity

The majority of bacteria are not able to metabolize triclosan [Vao and Salkinoja-Salonen, 1986; Liaw and Srinivasan, 1990; Schmidt et al., 1992, 1993]; therefore triclosan is detectable in aquatic ecosystems, sediments and sewage sludge [Tulp et al., 1979; Hites and Lopez-Avila, 1979; Lopez-Avila and Hites, 1980; Miyazaki et al., 1984; Paxéus, 1996]. Voets et al. [1976] described a 50% degradation of triclosan in an activated sewage model within 3 weeks. Further information regarding biological degradation was published by Hundt et al. [2000], Hay et al. [2001], Meade et al. [2001], McBain et al. [2003] and Schultz [2004]. Paxéus [2004] detected a degradation rate of >90% in biological sewage systems. Even under anaerobic conditions (sludge decomposition) a degradation of about 35% is possible [Räuchle, 1987].

Due to the high rate of photodegradation with a half-life of 3 h in summer [Räuchle, 1987], concentrations in surface water of 50 ng/l are substantially low [Singer et al., 2002].

Triclosan in sewage can exert negative effects on freshwater algae, nitrifying bacteria [Wilson et al., 2003; Dokianakis et al., 2004] and fish [Räuchle, 1987].

Concentrations up to 2 mg triclosan/l (limit of solubility) in sewage did not negatively influence the biological treatment of the sewage plants. Triclosan is

highly toxic to fish (LC_{50} at 48 h dwell period 0.6 mg/l, threshold for harmfulness approx. 0.4 mg/l). In shorter dwell periods higher concentrations are tolerated, e.g. 10 mg/l at 5 min, 5 mg/l at 15 min, 2 mg/l at 30 min. The degradation products, which are induced under the influence of light, are less toxic to fish. In reality the concentrations appearing in sewage are at least 1 or 2 log steps below the LC_{50} [Räuchle, 1987]. Plants can accumulate triclosan [Nishina et al., 1991; von Woedtke et al., 1999].

The possibility of contamination of triclosan-containing products with dioxin represents a critical issue. Therefore any contamination with furans and dioxins has to be excluded, and a negative declaration by the manufacturer is required.

Other Biocides

Other relevant substances used for the impregnation of textiles are silver and copper compounds, chitosan, zeolites, quats, imidazoles, imidazolidinones, isothiazolines, curcumin, thujopsene, hinokitiol (from cypress oil), sulfadiazine, 1,3-dimethylol-5,5-dimethylhydantoin, thiobisphenol, neomycin and dimethyltetradecyl [3-(trimethoxysilyl)propyl]ammonium chloride and polyhexamethylene biguanide hydrochloride (polyhexanide) [Sun et al., 2001; Nakashima et al., 2002; Takai et al., 2002; Qian and Sun, 2003, 2004; Thiemann, 2004; Han and Yang, 2005; http://www.der-gruene-faden.de/ teyt/text2497.html, www.bgw.de]. As scientific data are difficult to obtain, the following characteristics (tables 4–6) are incomplete and underline the need for further scientific evaluation and documentation.

The problem of different activities obtained with various textiles is exemplarily described in the following experiments.

The textile was cut into small pieces (2 × 2 cm), autoclaved after washing with household laundry detergent, dried and incubated with test organisms. After exposure, viable bacterial cells were counted. Relative humidity was maintained at 100% for wet conditions and 50% for dry conditions at 22°C.

Under dry conditions Gram-negative rods rapidly lost their viability. Ag. Zn, ammonium zeolite and chitosan were proven to be effective against *S. aureus* for up to 6 h of incubation under wet and dry conditions, and also effective against MRSA for up to 24 h only under wet conditions (table 7). The results indicated significant differences between the tested textiles; therefore products should be tested by use of the same standard; however, a DIN EN ISO is presently not available.

Surprisingly silver and copper exhibit marked differences in tolerance although both are heavy metals with partly comparable chemical properties (table 5). In the aquatic toxicity these differences are not primarily remarkable (table 6).

Table 4. Spectrum of activity of selected biocides for textile impregnation

Agent	Bacteria[1]		Fungi[1]	Resistance
	Gram-positive	Gram-negative		
Triclosan	active	lack of activity	active	in vitro inducible
Silver	highly active	highly active	highly active	no data
Quats	active	lack of activity	lack of activity	in vitro inducible
Chitosan	active	active	active	no data
Polyhexanide	active	active	active	no data
Copper compounds (e.g. sulfide and sulfate)	active	active	active	positive [Aarestrup et al., 2002; Hasman and Aarestrup, 2002, 2005; Ugur and Ceylan, 2003]

[1]Studies on antimicrobial activity are not comparable due to differences in methodology.

Silver

The therapeutic activity of silver has been known since the 5th century. Ciro the Great ordered his troops to transport water in silver pots to protect the drinking water against spoilage and to preserve its potability.

In contrast to triclosan, nanocristalline silver is equally active against Gram-positive and Gram-negative bacteria, fungi and several viruses, and surpasses triclosan by antimicrobial activity [Thurman and Gerba, 1989; Ugur and Ceylan, 2003]. The concentration of 0.2 μg Ag/ml eradicates the amount of *E. coli* by 2 log steps within 13 min [Wuhrman and Zobrist, 1958]. After 3 h no bacterial growth was detectable on a polyurethane catheter contaminated with 10^9 CFU of *E. coli, P. aeruginosa, Enterobacter cloacae, Citrobacter freundii, C. albicans* or *Candida glabrata* [Guggenbichler, unpubl.].

Ag^+ is highly toxic to fish (table 6). The key mechanism of acute silver toxicity consists in the reduction of Na^+ uptake by blocking of Na^+, K^+-ATPase [Bianchini et al., 2002]. Like other metals, silver accumulates in aquatic food chains and may exert toxicity, which cannot be predicted from exposure to dissolved Ag^+ [Hook and Fisher, 2001].

For impregnation of textiles, silver can be anchored on fiber polymers so that the silver is not removable from the fibers. As long as no silver is released, no toxic risks are given.

Quaternary Ammonium Compounds

The attachment of a quat to silk fibers could be realized by its polymerization. This new tissue combines the favorable properties of silk with protection

Table 5. Tolerance to selected textile biocides

Agent	Dermal resorption	Toxicity	Allergenicity	Mutagenicity	Carcinogenicity	Teratogenicity
Triclosan	yes	little to nontoxic	low	neg.	neg.	neg.
Silver	no	depends on liberation of compound: little to nontoxic	no	neg.	neg.	neg.
Quats	yes	moderate to highly toxic	moderate	neg.	neg.	neg.
Chitosan	no data	no hint (biologically deduced)	no	neg.	no data	no data
Polyhexanide	no	little to nontoxic	no	neg.	neg.	no teratogenic hazard to humans
Copper compounds (e.g. sulfide and sulfate)	no	essential trace element, dose-dependent toxicity	no	partly neg., but potentially mutagenic [Agarwal et al., 1989]	not cocarcinogenic [Sunderman et al., 1974]	neg. (2 mg Cu/kg) to rats [Mason et al., 1989] and humans [Kahn-Nathan, 1975; Barash et al., 1990], pos. to crab and copepods at environmental concentrations [Fisher and Hook, 2002; Lavolpe et al., 2004], shrimp [Rayburn and Aladdin, 2003] and *Chironomus tentans* [Martinez et al., 2003]

Table 6. Ecotoxicity of selected textile biocides

Agent	Biodegradation	Aquatic toxicity
Triclosan	slow	high toxicity for fish, modified behavior and growth of *Rana pipiens* in OWC concentrations [Fraker and Smith, 2004], 48-hour EC_{50} to *Daphnia magna* 340 μ/l, 96-hour LC_{50} to *Pimephales promelas* and *Lepomis macrochirus* 260 and 370 μ/l, respectively, NOEC and LOEC to *Oncorhynchus mykiss* 34.1 and 71.3 μ/l [Orvos et al., 2002]; 96-hour LC_{50} for 24-hour-old larvae of *Oryzias latipes* 602 μg/l, increased concentration of hepatic vitellogenin (estrogenic effect) at 20 μg/l with adverse effects in F_1 generation [Ishibashi et al., 2004]
Silver	no	$AgNO_3$ 48-hour LC_{50} to *Ceriodaphnia dubai* 0.5 μ/l, 8-day LC_{50} 0.32 μ/l, NOEC of silver cysteinate <0.001 μg/l, LOEC of $AgNO_3$ and silver glutathionate 0.01 and 0.6 μ/l, respectively [Bielmyer et al., 2002], 96-hour LC_{50} 330–2,700 μg/l to trout *Oncorhynchus mykiss* in seawater and 5–70 μg/l in freshwater [Hogstrand and Wood, 1998]
Quats	depends on structure: slow to rapid	dependent on structure: highly toxic
Chitosan	good	sublethal concentration to carp 75–150 mg/l [Dautremepuits et al., 2004]
Polyhexanide	no	highly toxic to fish
Copper compounds	no	$CuCl_2$ *Lemna minor* EC_{50} 0.3–0.9 mg/l, 1 ppm sublethal to algae [Mal et al., 2002], sublethal concentration to carp 0.1 mg/l [Dautremepuits et al., 2004], LOEC in water 6.8–13.6 μg/l [Hsieh et al., 2004]

LOEC = Lowest observed effect concentration; NOEC = no observed effect concentration; OWC = organic wastewater contaminant.

from microbial colonization. At longer contact times nonpolymerized quats can be absorbed by skin [BIA, 1995]. On the basis of their LD_{50} (and their chemical structure) and depending on the application mode, quats can be qualified as mild to highly toxic [Kramer et al., 1985; Merck Schuchardt, 2001]. In vitro benzalkonium chloride, a frequently used quat, irreversibly damages ciliated nasal epithelia [Klöcker and Rudolph, 2000]. Also wound healing is retarded [Bolton et al., 1985]. Quats have a potential for sensitization. Benzalkonium chloride is highly toxic for aquatic organisms [Material Safety Data Sheet 1999], but the agent is degraded within 28 days [Zöllner et al., 1995]. The development of antibacterial resistance is possible [Rudolf and Kampf, 2003].

Resuming these data a prolonged dermatological evaluation of benzalkonium chloride is not justified [Kramer et al., 2003]. This is also valable for other non-polymerized quats. These findings cannot generally be transferred to polymerized quats but require adequate investigations of the long-term tolerance of humans as

Table 7. Antibacterial properties of antimicrobial-impregnated textiles [Takai et al., 2002]

Antimicrobial agent	Efficacy				
	S. aureus		MRSA		*P. aeruginosa*
	dry	wet	dry	wet	wet
Ag, Zn, Cu zeolite	++	++	–	++	+
Ag, Zn, ammonium zeolite	+++	+++[1]	–	++++[1]	++[1]
Aliphatic imide	–	–	–	+	+
Quat	–	–	–	+	+
Chitosan	+++	+++[2]	–	++[2]	++[1]
Without	–	–	–	–	–

– = Not effective; + = slightly effective; ++ = moderately effective; +++ = effective; ++++ = highly effective.

[1]Significantly decreased activity with organic load.

[2]No influence of organic load.

well as of the environment. Beside this, the stability against microbial degradation of the polymer in textiles during wearing and washing must be analyzed.

The use of quats in the treatment of atopic dermatitis reduced the SCORAD within 1 week from 43 to 30 ($p = 0.003$). The local score improved from 32 to 18.6 ($p = 0.001$), the controls remained unchanged [Ricci et al., 2004]. Further clinical trials and the comparison with other therapeutic options are warranted.

Due to the risk of resistance development, any attempts to combine e.g. cephalosporins with quats are not indicated [Kim et al., 2000].

Chitosan

Chitosan is nowadays used in wound dressings and textiles [Allan et al., 1984; Li et al., 1992; Hirano, 1996; Tokura et al., 1996; Lee et al., 1997; Nam et al., 2001].

Chitosan is the deacetylated compound of chitin [Lim and Hudson, 2004] and as natural biopolymer can be extracted from the shells of aquatic animals (crabs, shrimp shells). The amino group in the C2 position of the cationic glucosamine provides its antimicrobial activity [Chen et al., 2002; Al-Bahra, 2004] by binding to the bacterial cells [Knobelsdorf and Mieck, 2000; Takai et al., 2002; Al-Bahra, 2004].

In a quantitative suspension test, chitosan is highly active. In 10 min a 0.1% solution achieves a reduction of *S. aureus* and *P. aeruginosa* of ≥5 log, of

C. albicans one of ≥4 log [Weber, unpubl.]. It is noteworthy that in the test chitosan remained undissolved as suspension, a situation comparable to textiles.

A decrease in antimicrobial activity by up to 2 log steps is observed in the presence of hyaluronic acid, ascorbic acid and NaCl, which has to be taken into consideration for practical purposes.

No allergic reactions are reported at present [Knittel and Schollmeyer, 1998]. On the basis of the LD_{50} in the mouse of 16 g/kg BW orally, chitosan can be considered as nontoxic. Adverse effects were observed at concentrations of >2,000 mg/kg BW in rats [Kim et al., 2001]. In accordance with the results of toxicological investigations, wound dressings with chitosan and collagen were proven to be favorable [Ye et al., 2004]. Because the agent is used for food conservation and weight reduction (weight loss supplements), no toxicity for impregnated textiles can be expected. In vitro tests with tissue cultures (hepatocytes) assumed this point of view [Risbud et al., 2003]. Furthermore, chitosan is antigenotoxically active by adsorbing mutagens [Ohe, 1996].

Chitosan is biodegradable and bioabsorbable [Pascual and Julia, 2001; Al-Bahra, 2004] and can be expected to play a role in the antioxidative mechanism of biological systems [Xue et al., 1998].

Zeolites

Zeolites are composed of silicium and aluminium tetrahedrons. By oxygen bridges these form secondary complexes agglomerating to tertiary tetrahedrons. Thereby a crystal structure with an extensive system of pores and channels is formed. As ion exchangers zeolites are endowed with antimicrobial agents, e.g. silver for impregnation of catheters and textiles [Thom et al., 2003].

Zeolites are not water soluble. The basic structure is nontoxic. In sewage sludge zeolites are degraded to silicic acid (http://sodasan.com/diplomarbeit/Pla-compaktp4.htm'#T3). Toxic and ecotoxic properties of zeolites originate exclusively from the coupled biocides.

Polyhexanide

The cationic and polymeric structure of the agent allows it to bind strongly to cellulosic fabrics such as cotton and viscose [Payne, 1997]. The good activity against both Gram-positive and Gram-negative bacteria has led to its use on cotton wound dressings and drain sponges. Cotton gauze containing polyhexanide has been found to be an effective barrier to bacterial penetration, even in the presence of protein [Reitsma and Rodeheaver, 2001]. A dressing substantially reduced (by 4 or 5 log) the amount of *P. aeruginosa* that had gained access to the wound bed and reduced the bacterial inoculum in the dressing itself. The presence of polyhexanide did not prevent epithelialization of partial-thickness wounds.

A repeated-insult patch test effectively demonstrated that the polyhexanide-treated gauze is devoid of skin-sensitizing properties [Orr et al., 2001].

Copper

On the basis of its broad antibacterial and antifungal activity, this agent was used in surgical gloves, filters, socks and antimite mattresses. In animal experiments no potential for sensibilization was detected [Borkow and Gabbay, 2004]. While copper is nonmutagenic for mammals, the compound is teratogenic and embryotoxic for aquatic organisms (table 6). For the estimation of ecotoxicity the evidence of available investigations in mammals is not sufficient. With the use in filters as exception, the clinical application of this agent is questionable.

Obsolete Compounds

The following agents, which have been described by Wigert et al. [1974] for use as antimicrobial impregnation of household and technical textiles, are considered obsolete: hexachlorophene, chlorphenols, organomercury, -tin and -zinc compounds, anorganic silver salts, hydroxychinolines, salicylanilides, dithiocarbamates, tetramethylthiuramdisulfide, neomycin and tetracycline.

In Germany *tributyl tin compounds* (TBT) are not allowed for antimicrobial impregnation of textiles. Otherwise, for heavy textile tissues, e.g. tents, its use is allowed. Due to its environmental burden this use has also to be dismissed because of its estrogen-like activity.

The concentrations of TBT in textiles ($<$110 mg/kg) are below the microbicidal concentration of 0.1% and derive from stabilizers and catalysts. Their maximal concentrations, which are reached by dermal absorption, are clearly below the tolerable daily intake value recommended by the WHO (www.bgvv.de, TBT and other organic tin compounds in foodstuff and consumer products, March 6, 2000). This evaluation solely takes the isolated action of the compound on the organism into consideration, whereas in reality human exposure always results from a mixture of compounds with unknown interactions. Because a toxicological analysis of various combinations with TBT has not been performed, a final risk assessment is not possible. For safety reasons, TBT generally has to be abandoned also as auxiliary material for textiles.

Textiles, manufactured in Germany, can be assumed as free of insecticides, pesticides and fungicides. In imported textiles these agents cannot be excluded because of the application for protection of moulding and bacterial destruction, especially as impregnations in tropical climates. Especially in imported textiles from developing countries, antimicrobial compounds, restricted in the EU, can be found, since only polychlorated phenols (e.g. pentachlorphenol) are forbidden for import materials. To remove unwanted residues, it is generally recommended

to wash, to clean and to air imported textiles before wearing (http:// www.swiss-textiles.ch/boxalino/files/Document183file.pdf).

Odor-Absorbing Agents

Cyclodextrin

Cyclodextrins are natural hydrophilic complex-building agents, which absorb odors without antimicrobial activity. Since 2000 these compounds have been allowed as food additives [Buschmann et al., 2001, 2003; Knittel et al., 2004]. As long as these compounds are not combined with biocides (e.g. with isothiazolinone), they can be used without risks for humans and the environment.

Conclusion

For toxicological reasons for humans and the environment the addition of so-called antismell agents with antimicrobial properties to textiles for daily use has to be avoided. Smelling textiles have to be returned to hygienic conditions, e.g. by washing. Textiles impregnated with antismell agents tend to be cleaned less frequently with the result of loss of functional quality. For the intended inhibition of malodor, deodorants or antiperspirants are the agents of choice.

Insofar as therapeutic or prophylactic advantages of antimicrobial textiles are proven and this application is at least equally effective and tolerated compared to conventional therapeutic options, no objections against their use can be made. In any case the used biocide has to be declared with documented efficacy. As these products represent almost medical devices or medicinal products in case of addition of a drug to textiles in the near future, the conformity of the registration needs legal assessment by notified bodies or by the drug approval authorities [Kramer et al., 2005a, b].

At present, important deficits are to be mentioned:

- International norms for in vitro testing as well as for preclinical assessment (antimicrobial activity and tolerance) of antimicrobial-impregnated textiles are missing. Compared with the harmonized European norms for testing of disinfectants, this situation warrants an urgent amendment.
- As for medical devices, independently from the intended use, a declaration (agent and concentration) for antimicrobial-impregnated textiles is requested. To prevent inappropriate use, a registration also for consumer products is wanted.
- For every agent a documented risk-benefit assessment has to be requested, including the intended application as well as the long-term tolerance by humans and the environment.

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