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Blood Chemistry Changes as an Evidence of the Toxic Effects of Anionic Surfactant Sodium Dodecyl Sulfate

M.A.M. Wadaan and M. Mubarak
Department of Zoology, College of Science, King Saud University,
P.O. Box 2455, Riyadh, 11451, Saudi Arabia

Abstract: The objective of the present study was to investigate the toxic, damaging and irritative effects of repeated exposure to Sodium Dodecyl Sulfate (SDS) on rabbit skin. The animals were exposed to 5% solution of SDS for 8 weeks through skin brushing. All exposed rabbits manifested dermatitis and they were dull, depressed, emaciated and their body weight was decreased. Blood chemical parameters including alkaline phosphatase (ALP), alanine transaminase (ALT), aspartate transaminase (AST), gama-glutamyl transferase (GGT), amylase, cholesterol, high density lipoproteins (HDLPs); triglycerides (TGs), creatinine, urea, glucose and potassium (K^+) were estimated after 8 weeks of SDS exposure. All blood parameters except ALP and creatinine were significantly increased or decreased as compared to that of the controls. It is concluded that topical application of SDS is capable of damaging the skin with all signs of dermatitis. Further, SDS is capable of being adsorbed and penetrates through the skin barrier and thus reaches the internal organs such as liver to provoke systemic damages. The estimated blood parameters can potentially serve as biomarkers for assessing SDS toxicity. However, further studies are warranted to confirm this hypothesis.

Key words: Sodium dodecyl sulfate, blood chemistry, rabbit

INTRODUCTION

The skin is the largest organ in the body, providing a protective barrier between the body external envirounent. The skin is exposed to a number of different chemicals and products, some of which have the potential to induce either irritating and/or allergic reactions (Fletcher and Basketter, 2006). Authorities of concern variously require data from skin patch testing in relation to the registration/classification of chemicals, cosmetic ingredients and drugs (Robinson *et al*., 2002).

Surfactants are widely used in everyday personal care and household products as well as in a variety of industrial applications (Li, 2008). In fact, many surfactants and their degradation products have been found worldwide in waste water discharges, sewage treatment, plant effluents, natural water and sediments (Ying, 2006). Because many surfactants are ubiquitous (Ying *et al*., 2002; Venhuis and Mehrvar, 2004), the potential toxic effects of these chemicals have attracted much research attention in the past several decades (Abel, 1974; Lewis and Suprenant, 1983; Lewis, 1991). Many different mechanisms of toxicities exist for different types of surfactants and one single surfactant can produce its toxicity through more than one mechanism (Li, 2008).

The toxicity of surfactants is primarily determined by their ability to be adsorbed and penetrating the cell membrane (Rosen *et al*., 2001). However, the molecular mechanisms of toxicities of surfactants are not well understood after their adsorption on the membrane surface. What is known is that an interaction with cell membrane lipids appears to disrupt membrane integrity, thus causing toxic effects (Abel, 1974).

Corresponding Author: Mohammad A.M. Wadaan, Department of Zoology, College of Science, King Saud University, P.O. Box 2455, Riyadh, 11451, Saudi Arabia

Anionic surfactants, such as Sodium Dodecyl Sulphate (SDS) are organic compounds that reduce water surface tension and are widely used in household detergent formulae. Intensive research has investigated the effects of surfactants on natural communities (Abel, 1974; Malagrino *et al*., 1987; Augier, 1991; Lewis, 1992; Huang and Wang, 1994; Hansen *et al*., 1997; Rocha *et al*., 2007; Rosety *et al*., 2007). SDS is commouly used as an active ingredient in household and personal care products as well as in specialized applications to fabrics, carpets and paper (Reuner, 2005; Li, 2008). Anionic surfactants such as SDS exert toxic and harmful effects on cell membranes and can solubilize proteins causing their denaturation (Cserhati *et al*., 2002; Lavoue *et al*., 2002).They can also modify the activity of an enzyme by binding to it (Cserhati *et al*., 2002).

The influence of SDS even in a very low concentration on physiological properties of the skin surface has been assessed. The induced changes in skin surface eventually cause injured barrier functions (Zahejsky *et al*., 1987). However, several studies have revealed the negative effect of the anionic detergent SDS on permeability barrier function (Agner and Serup, 1990; Frosch and Kurte, 1994; Fluhr *et al*., 2001). The present study was performed over 8 weeks to evaluate the irritation effects of SDS and to investigate the blood chemical changes in response to long-term SDS exposure.

MATERIALS AND METHODS

Animals

Adult domestic rabbits (4 months of age) weighing 2300-2450 g were obtained from the colony kept at King Saud University. The animals were maintained under the standard experimental conditions, including temperature (25°C), at the animal house, College of Science, King Saud University. Feed and water were available *ad libitum*.

Chemical Substance

Sodium dodecyl sulfate (SDS) [CH_3 $(CH_2)_{11}$ OSO_3 Na] (MW 288.38) (Wiulab Co., UK) was dissolved in distilled water and used at the concentration of 5% (w/v).

Experimentation

After one week acclimatization period, the animals were randomly divided into two groups, group 1 (exposed group) (n = 10, 5 males and 5 females) and group 2 (control group) (n = 8, 4 males and 4 females). Animals of the group 1 were exposed once daily to a gentle cutaneous application of SDS through a soft hair brush on the back region for 8 weeks (from mid October to mid December, 2004). The exposed area of the hair and skin was left to dry and thereafter washed with normal water. Control animals (group 2) were brushed with normal water and not exposed to SDS solution. Throughout the whole experimentation period, the exposed animals were observed for developing skin lesions or other clinical signs.

Blood Chemistry

Blood samples were collected from all experimental animals after 8 weeks of exposure to SDS. Serum harvested from the collected blood samples using an analyzer apparatus (Reflotron plus, Roche, Germany) using Reflotron kits (Roche Diagnostics, Germany) were used to estimate the various blood chemical parameters. The estimated parameters included alkaline phosphatase (ALP), alanine transaminase (ALT), aspartate transaminase (AST), gama-glutamyl transferase (GGT), amylase, cholesterol, high density lipoproteins (HDLPs); triglycerides (TGs), creatinine, urea, glucose and potassium ions (K^+).

Statistical Analysis

The obtained results were analyzed using the Student-Newman-Keuls multiple comparison test of ANOVA.

RESULTS AND DISCUSSION

Gross Findings

Hair loss (alopecia) was observed in the skin area of the back region of the animals that were exposed to SDS solution for 8 weeks. Severe signs of dermatitis along with dermal congestion, skin erosions and dermal crusts were also observed on the skin area exposed to SDS. Clinically, the SDS-exposed rabbits were dull, depressed, emaciated and their food consumption was markedly decreased. Consequently the body weight of the SDS exposed animals was reduced as compared to the controls.

Blood Serum Chemistry

Among the estimated blood chemical parameters, ALT was significantly ($p<0.05$) increased in the SDS exposed animals, whereas AST, GGT, amylase, cholesterol, HDLPs, TGs, urea, glucose and K^+ were significantly decreased as compared to the controls (Table 1). However, creatinine and ALP levels remained unaffected due to SDS treatment (Table 1).

The results of the present study clearly indicate that the repeated exposure of skin to SDS solution provokes skin damage. The current results have approved that adsorption and penetration of SDS through skin is such deep that it causes drastic alterations in the levels of blood chemical parameters. The toxic effects of the anionic detergent (surface-active) SDS has been reported by Dehelean *et al*. (2004), who applied SDS for a long-term using Spragne Dawley rats as an animal model. However, the induction of hypo-irritation with a prolonged exposure to known irritants such as SDS has not been fully studied by Widmer *et al*. (1994) and Wahlberg (1992). Well-known irritants are detergents, cleansing agents, hand cleansers, chemicals, cutting fluids and abrasives (Wigger-Alberti *et al*., 2002). Washing procedures such as hand washing at a high frequency, aggressive use of hot water (Berardesca *et al*., 1995; Clarys *et al*., 1997), scrubbing, cumulative exposure to one or more of the chemical irritants (Morris-Jones *et al*., 2002) and insufficient skin protection (Bauer *et al*., 2001) are among the common causes of irritant contact dermatitis. Daily exposure to such irritants induces significant changes in several parameters, which may reflect the direct cytotoxicity of the irritants and the skin's immunological naiveté (Branco *et al*., 2005). Most irritation parameters show a quick amplified response consistent with the proven concept of skin penetration after disruption of the skin barrier (Branco *et al*., 2005).

The mechanism behind the disruption of skin barrier by detergents, especially SDS, is thought to induce a decrease of lipid melting point and an increase in water diffusion (Ribaud *et al*., 1994). The

Table 1: Blood chemical parameters of rabbits whose skin was exposed topically to 5% sodium dodecyl sulfate solution once daily for 8 weeks

Parameters	Control (n = 10)	Exposed (n = 8)
ALP ($\mu L\ L^{-1}$)	96.70±13.41	81.10±4.36
ALT ($\mu L\ L^{-1}$)	24.83±2.66	31.63±0.46*
AST ($\mu L\ L^{-1}$)	37.40±1.73	10.83±2.44***
GGT ($\mu L\ L^{-1}$)	11.06±3.07	8.54±0.24*
Amylase ($\mu L\ L^{-1}$)	638.08±19.05	449.67±58.31***
Cholesterol (mg dL^{-1})	127.00±17.32	102.00±1.08**
HDLPs (mg dL^{-1})	15.13±0.68	9.83±0.29**
TGs (mg dL^{-1})	208.33±98.47	82.75±8.13***
Creatinine (mg dL^{-1})	1.22±0.12	1.11±0.09
Urea (mg dL^{-1})	55.20±1.73	22.50±1.39***
Glucose (mg dL^{-1})	282.00±15.59	104.00±6.93***
K^+ (mmol L^{-1})	8.41±0.20	7.14±0.44*

Values are expressed as Mean±SD. *$p<0.05$, **$p<0.01$ and ***$p<0.001$ compared to the control values evaluated by Student-Newman-Keuls multiple comparison test of ANOVA. ALP: Alkaline phosphatase, ALT: Alanine transaminase, AST: Aspartate transaminase, GGT: Gamma-glutamyl transferase, TGs: Triglycerides, K^+: Potassium ions

responsible mechanism involves disorganization of the intercellular lipids application of the detergents such as SDS on human skin. It has been concluded that SDS can induce damage of the skin barrier function (Lévesque *et al*., 1993). When applied topically, SDS is considered an acute irritant through its direct cytotoxic effect on keratinocytes and thus affecting both lipid and protein structures. The stratum corneum, the outermost layer of the epidermis, is 10-20 μm thick in most surfaces on the human body (Pirot *et al*., 1997) and consists of 2 compartments, a desquamating layer of protein enriched corneocytes embedded in a compact lipid intercellular matrix (Elias, 1983). There are several pathways explaining how the molecules find their way into the stratum corneum. These pathways involve transcellular/intracellular diffusion and through shunt holes or shunts left by hair follicles, glands, skin appendages (Tanojo *et al*., 2001). Analysis of the mechanism responsible for penetration of the molecules through the stratum corneum is valuable for drug delivery research, as well as to assess the skin toxicity after exposure to a suspected substance.

Most of the blood chemical parameters studied herein, such as ALP, amylase, AST, cholesterol, TGs, HDLPs, are known biomarkers for hepatocellular damage (Chopra and Griffin, 1985).

It will be worth investigating further as to if the blood parameters studied herein returned to baseline, upon the discontinuation of SDS exposure. Conclusively, the present significant alterations in the normal levels of these blood chemical parameters due to topical exposure to SDS, evidently indicate that SDS is capable of deep adsorption and penetration through the skin barrier and can reach deeper internal organs such as liver and kidneys to inflicting systemic effects. The present findings lay a possibility for further studies to establish such deleterious effects of SDS on liver and kidneys.

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