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Silibinin as a potential therapeutic for sulfur mustard injuries

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Sulfur mustard (SM) is a vesicating chemical warfare agent causing skin blistering, ulceration, impaired wound healing, prolonged hospitalization and permanent lesions. Silibinin, the lead compound from Silybum marianum, has been discussed as a potential antidote to SM poisoning, but previous investigations had been limited to nitrogen mustards. Water solubility of silibinin is poor, thus a water-soluble prodrug, e.g. silibinin-bis-succinat (silibinin-BS, SIL-BS) should be desirable for rapid bioavailability as an antidote. HaCaT cells were exposed to SM (30, 100, and 300 µM) for 30 min and treated thereafter with SIL-BS (10, 50, and 100 µM) for 24 h. Necrosis, apoptosis and production interleukin-6 and -8 were determined. SIL-BS dose-dependently reduced SM cytotoxicity, even after 300 µM exposure. Doses of 50-100 µM SIL-BS were required for significant protection. Apoptosis and interleukin production remained largely unchanged by 10-50 µM SIL-BS but increased slightly after 100 µM treatment, in particular when cells had previously been exposed to 300 µM SM. HaCaT cells, incubated with SIL-BS were lysed and investigated by LC-ESI MS/MS. Findings suggest that SIL-BS is absorbed by HaCaT cells and biotransformed into free silibinin. In summary, silibinin-BS is a promising compound for the treatment of SM injuries: biotransformation to free silibinin is possible and standard doses for clinical use (50-100 µM) provided a significant reduction of necrosis. At doses of 50 µM SIL-BS, no pro-inflammatory or pro-apoptotic effects occurred, but even pro-apoptotic effects of 100 µM SIL-BS were observed only after 300 µM SM exposure and might even be useful to eliminate cells with irreversible SM-induced damage.

Biography

F Balszuweit is a pharmacist and obtained his PhD at the Free University Berlin in 2005. Along with his research activities within the Bundeswehr Medical Service, he has been concerned with research management, regulatory affairs and scientific cooperation. His research interests are focused on cell co-cultures to identify novel treatment strategies, in particular against sulfur mustard injuries.

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