Laboratory of Renal Lithiasis Research, Institute of Health Sciences Research (IUNICS), University of Balearic Islands, Palma de Mallorca, Spain

Absorption of myo-inositol hexakisphosphate ($InsP_6$) through the skin in humans

F. Grases, B. Isern, J. Perelló, P. Sanchis, R. M. Prieto, A. Costa-Bauzà

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Prof. Dr. F. Grases, Laboratory of Renal Lithiasis Research, Faculty of Sciences, University of Balearic Islands, 07122 — Palma de Mallorca, Spain
fgrases@uib.es

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In this paper, we present a pilot study of the absorption of myo-inositol hexakisphosphate ($InsP_6$) through the skin in humans. We found that, after topical treatment with a 4% $InsP_6$ rich gel, $InsP_6$ urinary excretion increased 54% compared to the control situation (participants submitted to an $InsP_6$-poor diet for 15 days, $n = 6$), clearly demonstrating that $InsP_6$ is absorbed through the skin of humans. These results demonstrate the topical application as a suitable administration route of $InsP_6$ in humans.

Myo-inositol hexakisphosphate (phytate, $InsP_6$) is a molecule to which several beneficial properties have been recently attributed. Some of these properties are related to its dermatological use. Thus, it has been claimed the capacity of $InsP_6$ to inhibit skin cancer (Ishikawa et al. 1999; Gupta et al. 2003; Grases et al. 2005) and to avoid calcinosis cutis (Grases et al. 2005b). In spite of these facts, little is known about the dermal absorption of $InsP_6$ in humans. Previous studies demonstrated that absorption was observed when applying $InsP_6$ topically to rats, with urinary $InsP_6$ concentrations much higher than those found with $InsP_6$ ingestion (Grases et al. 2005b). It was also found that in rats, $InsP_6$ was absorbed through the skin using both a gel or a cream, demonstrating that its absorption is independent of the matrix used for the topical application (Grases et al. 2005b).

Twenty healthy volunteers (7 males and 13 females) were selected to study the dermal absorption of $InsP_6$ in humans. Due to the direct relation between serum $InsP_6$ concentration and its urinary excretion (Grases et al. 2001), this last parameter was used to evaluate $InsP_6$ dermal adsorption. The experiment had two phases. In the first one, all participants were submitted to an $InsP_6$-poor diet for 15 days (all types of integral cereals and integral cereal derivatives, integral rice, corn, legumes, all types of nuts and other vegetable seeds were totally excluded). It has been demonstrated that $InsP_6$ levels in biological fluids and mammalian tissues clearly depend on dietary intake, consequently these levels must be low after this first period. On the 15th day, early in the morning (7 : 00) volunteers voided the urine accumulated overnight in the bladder and after two hours fasting, urinary samples were collected (2 h-urine). Then, the subjects began the second phase of the experiment. They continued with an $InsP_6$-poor diet and were topically treated twice a day with 10 g of a standard moisturizing gel with a 4.0% content of $InsP_6$ as potassium salt (Table). The surface of treatment was about 1400 cm^2. Urinary samples were again collected at the 7th day of treatment to evaluate $InsP_6$ excretion (2 h-urine). The experimental procedure was approved by the bioethics committee of the University of Balearic Islands. The obtained results are shown in the Fig.. As it can be observed, after topical treatment with $InsP_6$ rich gel, $InsP_6$ urinary excretion increased by 54%. That result clearly demonstrated that $InsP_6$ was absorbed through the skin layers of humans, crossed the epidermis, arrived to the dermis, entered the blood stream and increased urinary excretion. From the presented results, it can be deduced that topical administration of $InsP_6$ to humans can increase its concentrations in tissues and biological fluids, this demonstrating that the topical application, can be proposed as a new administration route of $InsP_6$ in humans.

Table: Composition of the moisturizing gel containing 4% of phytate as potassium salt

Component	Percentage composition
Water	86.4
Propylene glycol	6
PNC 400	2
Astro C-40	0.2
Potassium phytate	5.4 (4% $InsP_6$)

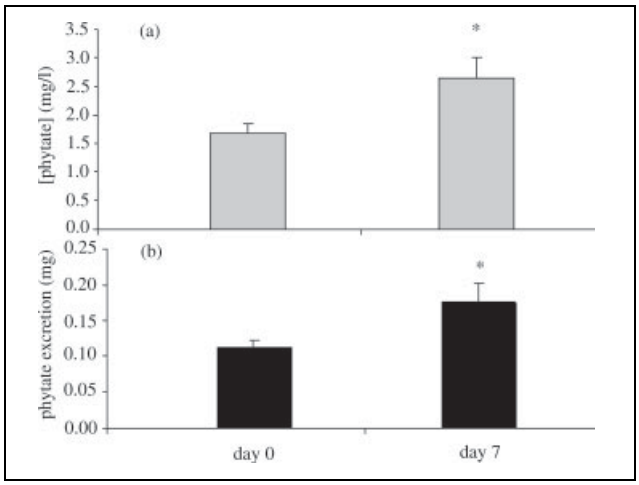

Fig.: (a) Urinary phytate concentration (mg/l) and (b) urinary phytate excretion (mg/2 h) at day 0 (before treatment) and at day 7 (after $InsP_6$ rich gel application). Values are mean of 20 subjects. Student's t-test was used to determine statistic significance between means. Error bars represent SE (* $p < 0.05$ vs day 0)

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