Skin Metabolism and Skin Sensitization...

Prof. Jean-Pierre Lepoittevin University of Strasbourg

> 2nd Skin Metabolism Meeting Valbonne, October 10-11, 2013





• • • The Skin...

Highly symbolic organ...

The first molecular interface with our environment...





•••• Skin and Toxicology....

Interaction of exogenous molecules with skin structures can lead to toxic reactions...





Allergic Contact Dermatitis

Skin inflammatory reaction mediated by the immune system... resulting from the interaction

of a low molecular weight exogenous chemical with endogenous skin proteins...





STUDIES ON THE SENSITIZATION OF ANIMALS WITH SIMPLE CHEMICAL COMPOUNDS. II

BY K. LANDSTEINER, M.D., AND JOHN JACOBS, M.D.

(From the Laboratories of The Rockefeller Institute for Medical Research)

(Received for publication, June 10, 1936)















Contact Dermatitis 2006: 54: 73–74 Printed in Singapore. All rights reserved Copyright © Blackwell Munksgaard 2006

CONTACT DERMATITIS

Editorial

Metabolism *versus* chemical transformation or pro- *versus* prehaptens?



Metabolic activation...



Abiotic activation...

















• • • The cinnamic alcohol story...



cinnamic alcohol

cinnamic aldehyde

- Cinnamic alcohol was considered as "The model" of prohapten for many years...
- Many metabolic studies performed...
- Clinical data available...







cinnamic alcohol

cinnamic aldehyde

- Cinnamic alcohol was considered as "The model" of prohapten for many years...
- Many metabolic studies performed...

Not all patients sensitive to cinnamic alcohol are ** reacting to cinnamic aldehyde !



• • • The cinnamic alcohol story...









• • • The corticosteroids story...





R = OH Hydrocortisone R= H Cortexolone

R = OH 21-Dehydrocortisone R = H 21-Dehydrocortexolone

Strong antiinflammatory properties...



Potent skin sensitizer in Human...

Matura et al. Contact Dermatitis 1998, 38, 106





• • The corticosteroids story...

Many poly-sensitized individuals also present a positive patch-test reaction to ethanol...





By courtesy of Prof. An Goossens





Dooms-Goossens A. Eur J Dermatol 1993, 3, 713





Liver metabolism...



Skin metabolism...













Liver vs skin...



Highly reactive intermediates...





• • • Non invasive approach...

Direct
observation...
Highly non
homogeneous
environment...











- High-Resolution Magic Angle Spinning NMR...
- Bring to zero inhomogeneity associated with the sample...
- NMR technique adapted to semi-solid structures...
- Developed for biopsies of soft tissues...





• • HR-MAS NMR on RHE (SkinEthic[®])



• • • HR-MAS NMR on RHE (SkinEthic[®])







• • HR-MAS NMR on RHE (SkinEthic[®])





















Moss E., et al. unpublished results



Hapten-protein interactions...



• • • Conclusions

- Most chemicals are detoxified through metabolism...
- Reactive intermediates can modify proteins and induce skin allergies...
- Skin metabolism associated with hapten formation is difficult to investigate...
- Mechanisms associated are mainly unknown...





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