

increased, providing proof that the increased NAD content was due to topical delivery.

In another experiment, the effect of the number of daily application of 1% tetradecylnicotinate cream was examined. Again, application was made to the back of the animal and the abdomen of each animal served as control. The results, depicted in FIG. 16, show that the NAD content of skin removed from the back increased as a function of the number of daily applications. In contrast, the NAD content of the abdomen did not increase, providing additional evidence that the increased NAD content was due to topical delivery of the pro-NAD agent.

It should be noted that in no case were any signs of toxicity observed as a result of the topical application of tetradecylnicotinate cream in the experiments shown in FIGS. 15 and 16.

Other pro-NAD agents may be identified by exposing cells in culture to candidate pro-NAD agents or by exposing skin on a test subject, such as a mouse, to the candidate pro-NAD agent. After a safe and effective dosage is determined, the candidate pro-NAD agents may be tested on human volunteers and assayed by skin biopsy samples. The effectiveness of the pro-NAD agents may be determined by (a) biochemically analyzing cell lysates to assess the cellular NAD content or (b) scoring phenotypic or functional changes in treated cells as compared to control cells that were not exposed to the candidate pro-NAD agent.

Where analogs and derivatives of a known pro-NAD agent are to be identified or evaluated, the cells are exposed to the pro-NAD agent of the invention and compared to positive controls which are exposed only to the known pro-NAD agent, and to negative controls which were not exposed to either the candidate pro-NAD agent or the known pro-NAD compound.

In order to determine if the pro-NAD agent administered according to the method of the invention is absorbed into body tissues, and if so, in which tissue absorption occurs, the following may be performed. Samples of various body tissues from a subject, such as a laboratory mouse, were analyzed for NAD content at increasing hours after oral administration of a pro-NAD agent. The results of the measurement are compared to that of control subjects to determine the percent increase of NAD content. A dose response curve and a therapeutic index can be developed to determine the optimal oral dosage.

Other embodiments and uses of the invention will be apparent to those skilled in the art from consideration of the specification and practice of the invention disclosed herein. All U.S. patents and applications and other references noted herein are specifically incorporated by reference. The specification and examples should be considered exemplary only with the true scope and spirit of the invention indicated by the following claims.

We claim:

1. A composition for increasing intracellular NAD content, consisting essentially of n-tetradecyl nicotinic acid ester and a pharmaceutically acceptable carrier.

2. The composition of claim 1, wherein said n-tetradecyl nicotinic acid ester is presented in id composition at from about 0.001% to about 10% by weight of said composition.

3. The composition of claim 2, wherein said n-tetradecyl nicotinic acid ester is present in said composition at from about 0.01% to about 3% by weight of said composition.

4. The composition of claim 3, wherein said n-tetradecyl nicotinic acid ester is present in said composition at about 1% by weight of said composition.

5. A composition for increasing intracellular NAD content consisting essentially of:

- (i) n-tetradecyl nicotinic acid ester;
- (ii) an antioxidant, a sun screen, a vitamin or a pH stabilizer, and
- (iii) a pharmaceutically acceptable carrier.

6. The composition of claim 5, wherein (ii) is an antioxidant.

7. The composition of claim 5, wherein (ii) is a sun screen.

8. The composition of claim 5, wherein (ii) is a vitamin.

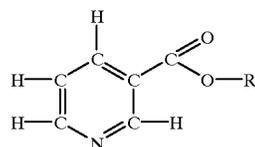
9. The composition of claim 5, wherein (ii) is a pH stabilizer.

10. The composition of claim 5, wherein (i) is present at from about 0.001% to about 10% by weight of said composition.

11. The composition of claim 10, wherein (i) is present at from about 0.01% to about 3% by weight of said composition.

12. The composition of claim 11, wherein (i) is present at about 1% by weight of said composition.

13. A composition for increasing intracellular NAD content, comprising a compound of formula:



wherein R₁ is an alkane group of 14 to 22 carbon atoms which also contains at least one functional group selected from the group consisting of a thiol, alcohol, amine, carboxylic acid, onium, carboxylic anhydride, carboxylic ester, acyl halide, amide, nitrile, aldehyde, ketone, imine, ether, sulfide, halide, nitro, nitroso, azide, and diazo group, and a pharmaceutically acceptable carrier.

14. The composition of claim 13, wherein R₁ is an alkane of 14 carbon atoms.

15. The composition of claim 13, wherein said compound is present at from about 0.001% to about 10% by weight of said composition.

16. The composition of claim 15, wherein said compound is present at from about 0.01% to about 3% by weight of said composition.

17. The composition of claim 15, wherein said compound is present at about 1% by weight of said composition.

18. The composition of claim 13, further comprising an antioxidant, a sun screen, a vitamin, or a pH stabilizer.

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