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SUNBURN PREVENTIVE AND BURN REMEDY

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This invention relates to a pharmaceutical preparation for oral administration and is primarily directed to a composition of matter for preventing and counteracting, or in some instances relieving, the effects upon the human skin and subcutaneous tissues of burning, particularly sunburn to which many are susceptible on exposure to the sun following a period of little or no exposure.

Some persons by exposing the skin gradually to sunlight develop pigmentation therein which if carefully built up affords substantially complete protection against the effects of further exposures for a considerable period, but others do not acquire such pigmentation or "tan" and suffer painful and otherwise harmful effects on even relatively brief direct exposure. The precise chemistry of these phenomena is not known, but it has been found that certain substances compounded with lotions, creams, ointments and the like on external application to the skin do afford some sunburn protection, perhaps due to their opacity or optical density to rays of those wave-lengths in sunlight ranging from about 2900 to 3260 Angstroms believed to be the principal cause of sunburn. Whether the natural pigmentation following gradual exposure to the sun in those persons who thereby become tanned produces in a layer of the skin a similar opacity or optical density or by some other effect renders the skin relatively immune to sunburn has not, so far as I am aware, been ascertained but it is generally recognized that local external application of sunburn preventives is acceptable to many only because other more convenient protection is not available.

In accordance with the present invention internal medication, administered orally, affords substantially complete protection from sunburn on subsequent exposure to the sun and promotes relatively rapid development of pigmentation in the exposed skin layers whereby after the tanning process has been completed the effects of further exposure following interruption of the medication are resisted substantially as if the tan had been developed naturally by gradual exposure, for example, during several successive days and for increasing times. Persons whose skin does not tan naturally obtain generally like protection, although they may find it advisable to continue the medication prior to exposure each day if little or no tanning or other enduring resistance to the effects of sunlight develops, and these latter find occasional ingestion of a medicament more convenient and effective than external application of sunburn preventives.

Moreover, my novel composition has been found to afford prompt relief of pain and to induce subsidence of other effects of skin burns resulting from heat alone where the ultraviolet rays in sunlight are not involved.

Compositions intended for producing these effects have long been sought and some have seemed experimentally to suggest as an effective constituent 8-methoxy psoralen (8-MOP) which has been contained in remedies in use since early times for relief of vitiligo, a condition of the skin characterized by local or general pigmentation deficiencies causing cosmetic disfiguration. Efforts to produce an effective potential sunburn preventive for oral ingestion with this compound as a base, however, have revealed that its toxicity in quantities sufficient to produce a normal tan on exposure to the sun is such that it cannot safely be tolerated by many persons, while combining it with other substances selected for their capacity to reduce its

toxicity impairs its effectiveness and produces other unacceptable responses as "side effects." Consequently while preparations containing 8-MOP may afford to some persons some degree of protection against sunburn without producing other effects deemed harmful or causing physical discomfort, the incidence of the latter among persons not resistant thereto renders such preparations unsuitable for general distribution in the trade.

I have found, however, that para aminobenzoic acid (PABA) properly administered has effectiveness following its ingestion comparable to that of 8-MOP in respect to affording protection against sunburn and while it cannot satisfactorily be administered alone for this purpose, when combined with certain other ingredients the sunburn protection properties of PABA are retained and even intensified yet without the undesirable side effects its administration alone sometimes produces.

The combination with PABA of said other ingredients as hereinafter more fully described thus affords a medicament for oral administration which when a standard dose is ingested an hour or so before initial exposure to the sun and thereafter at times during such exposure provides protection against sunburn, without observable side effects, and when ingested after exposure to sun or other burning of the skin, affords quick relief of the pain of the burn and prompt subsidence of the resultant vesiculation.

It is therefore a principal object of the invention to provide a novel composition of matter which when ingested by the human body affords to it the capacity to resist the pain and vesiculation normally associated with and flowing from prolonged exposure to sunlight thereby obviating preliminary preparation therefor as by initial gradual exposure over several successive days to develop natural tan and/or external topical application of sunburn preventives, said composition also affording effective relief when burning has occurred either from exposure to the sun or otherwise before, or within a very short time after, ingestion of the composition.

A further object is to provide a composition containing PABA and other ingredients which when ingested, preferably by administration in tablet form, counteract certain effects of PABA administered alone but without impairment of its specific property of temporarily immunizing the body from the effects of sun exposure and other burns.

Other objects, purposes and advantages of the invention will hereinafter more fully appear or will be understood from the following more specific description of the nature and ingredients of my composition, the preferred manner of its use and its principal effects when administered orally.

While PABA has long been known and about 1940 was recognized as a member of the vitamin B complex, its use in therapy has been confined to administration of massive doses of 6 to 24 grams daily for treatment of such conditions as premature canities, certain dermatoses including various hair and scalp diseases and rickettsial diseases, among them Rocky Mountain spotted fever; moreover PABA conjointly with salicylates other than aspirin has been considered beneficial in the treatment of rheumatic fever and arthritis while its use as a "sunscreening" agent in solutions, creams and ointments for topical application has also been suggested.

Oral administration of PABA in the quantities recommended in the literature, however, has produced occasional undesirable side effects including nausea, vomiting and anorexia while fever and dermatitis medicamentosa have also been observed on occasion following such treatments. But substantial reduction in the dosages of PABA in treatment of these various disorders has been considered unproductive of any positive results.

In the utilization of the composition of my invention,

however, PABA is administered in such manner as to introduce by ingestion not in excess of about 300 mg. per day and accompanied by other agents which greatly enhance the effectiveness of the PABA in affording protection from the sun while inhibiting undesirable side effects often accompanying the administration of large amounts of PABA alone.

More specifically, I combine in tablet form, approximately 75 mg. of PABA, 6–50 mg. of an antihistaminic agent and about 300 mg. of a suitable salicylate, preferably aspirin, together with a small quantity of a relatively inactive hygroscopic bonding agent such as starch, and it may sometimes be deemed desirable to include an alkaline reagent such as $MgCO_3$ in the proportion of about 2:1 to the weight of PABA merely as a neutralizing agent to counteract the acidity of the other ingredients.

These tablets are administered orally in quantities not to exceed 4 per day preferably the initial dose of one tablet being taken not less than 1 hour before exposure to the sun under conditions which might otherwise cause sunburn and like doses thereafter at 4-hour intervals. If the exposure is prolonged and repeated on successive days it is particularly advisable the tablets be taken at the said rate until a tan adequate to afford full protection against subsequent sunburn has developed, at which time further medication becomes unnecessary.

The combined effects of the several agents incorporated in tablets administered orally as described is to promote "tanning" of the skin on exposure to sunlight and inhibit the pain and vesiculation normally among the after-effects of prolonged exposure of untanned skin thereto yet without the tightening or dryness of the skin which has been noted as attending exposure to sunlight after ingestion of PABA alone in any safe amounts.

My composition moreover is without any noticeable effect if its ingestion is not followed by exposure to sunlight or other burning except in those instances in which it is used as a remedy for burns suffered before its administration in which circumstance it produces a subsidence of pain usually in less than one hour, followed by reduction of vesiculation caused by the burn and rapid healing of the wound without appreciable discomfort to the patient, although of course it cannot restore to fully normal physical condition of mutual adherence skin layers which have been locally separated by vesiculation occurring before the medication has begun to have effect. Moreover, it of course will be appreciated that for whatever purpose the preparation is taken its effects do not appear instantly upon administration but only after a period of time sufficient to enable the constituents of the composition to enter into the physiological activity of the body.

While I have stated in terms of a fairly wide range the proportion of antihistaminic agent used in by composition this is necessitated by the absence of a common factor of effectiveness among the many antihistaminic agents available and the wide range of their effectiveness per unit of weight administered. A fairly accurate guide to the amount of such agent desirably combined in a tablet containing about 75 mg. PABA can be obtained from the U.S. Pharmacopeia, or from the National Formulary, accepting the former when these differ, wherein the recommended single adult dose of recognized antihistaminic agents is set forth; any such recommended dose is suitable for my purposes. Thus, for example, when "Neo-Antergan" Maleate (pyrilamine maleate) is the antihistaminic agent used about 50 mg. of it (as so recommended) should be combined with 75 mg. PABA and 300 mg. aspirin in each tablet, whereas smaller doses of other antihistaminic agents may be adequate. In this combination of an antihistaminic agent with PABA and aspirin the usual side effects of such agents are not noticed, the specific effects of drowsiness following antihistaminic agent therapy and increased sensitivity to sunlight following ingestion of aspirin being notably among those which do not appear.

It therefore follows that the several agents combined in my preparation coact in the body to afford resistance to or tolerance of exposure to sunlight and the effects of burning of the skin in a manner and to an extent not attainable by ingestion of any of them individually, any two successively or even all three taken separately and in non-cooperative relation. Ingested concurrently, and in substantially the proportions stated, however, they act conjointly, each perhaps in a measure counteracting certain of the effects of the others and in turn enhancing other effects whereby discomfort, internal disorders and peripheral pain and vesiculation on exposure to sunlight are avoided and semi-permanent immunity to sunburn quickly attained. The tanning which affords this immunity persists after cessation of the medication provided the tanned areas continue to be occasionally exposed to the sun sufficiently to prevent the normal fading and dissipation which occurs naturally, although gradually, when frequent exposure to the sun is discontinued.

Reference to the ingredients of my preparation and to its administration has herein been made in terms of milligrams (mg.) but it will be recognized that the weight ratios of the said ingredients may be expressed equally well in terms of any other unit and that the preparation may therefore be defined as comprising parts by weight of the several ingredients utilizing the same numerical ratios, to facilitate compounding it in bulk quantities.

While I have herein stated specifically the preferred composition of my preparation and the best mode now known to me for administering it, it will be understood that the medical profession recognizes equivalents in certain drugs of which insufficient knowledge is available to enable exact equivalency to be determined and it is therefore within the scope of my invention to employ instead of para amino benzoic acid certain salts of this acid, particularly its sodium and potassium salts, provided equal results are realized; also that while I prefer to use aspirin as an ingredient, other salicylates or closely related compounds such as may be determined to be equivalent thereto may be substituted, while other changes in the composition itself, as well as in the manner of administering it, will readily occur to those skilled in the art and may be adopted without departing from the spirit and scope of the invention as defined in the appended claims.

Having thus described my invention, I claim and desire to protect by Letters Patent of the United States:

1. A pharmaceutical composition consisting essentially of about 12 parts by weight acetyl salicylic acid, about 3 parts by weight para aminobenzoic acid and about 0.24–2 parts by weight of an antihistamine.

2. A tablet for oral administration comprising a mixture of solid components, said mixture consisting essentially of about 300 mg. acetyl salicylic acid, about 75 mg. para aminobenzoic acid and about 6–50 mg. of an antihistamine.

3. A method of preventing and treating the effects of sunburn which comprises orally administering a solid composition consisting essentially of about 12 parts by weight acetyl salicylic acid, about 3 parts by weight para aminobenzoic acid and about 0.24–2 parts by weight of an antihistamine, the total daily dose of para aminobenzoic acid being not in excess of about 300 mg.

4. A method of preventing and treating the effects of sunburn which comprises administering four equal doses per day of a solid composition consisting essentially of about 12 parts by weight acetyl salicylic acid, about 3 parts by weight para aminobenzoic acid and about 0.24–2 parts by weight of an antihistamine, the initial dose being administered at least one hour prior to exposure and the remaining three doses being administered at four hour intervals from the time of the first dose, the total amount of para aminobenzoic acid in all four doses not exceeding about 300 mg.

(References on following page)

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References Cited in the file of this patent

UNITED STATES PATENTS

2,768,115 Buckwalter et al. ------- Oct. 23, 1956

OTHER REFERENCES

Lesser: D. & C. 1., vol. 70, No. 6, June 1952, pp. 750–751 and 824–830.

Modern Drug Encyclo. and Therapeutic Index, 5th ed. (1952), Drug Publications Inc., New York, N.Y., pp. 695–696.

Goodman et al.: Pharmacological Basis of Therapeutics, 2nd ed. (1955), Macmillan Co., New York, N.Y., pp. 657–660.

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Mfg. Chemist, vol., 27, No. 12, December 1956, p. 515.

Zarafonetic: Ann. Ind. Med., vol. 30 (1949), pp. 1188–1211.

Best et al.: "Physiological Basis of Medical Practice," 6th ed. (1955), Williams & Wilkins, Baltimore, pp. 314–318.

The American Drug Index, Wilson et al., J. B. Lippincott Co., Philadelphia, Pa., 1956, p. 356.

J.A.M.A., June 9, 1956, vol. 161, No. 6, p. 565.