THE TREATMENT OF VITILIGO WITH AMMI MAJUS LINN*

A PRELIMINARY NOTE

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At the suggestion of our Egyptian colleagues we have used an extract of the plant *Ammi Majus Linn* in the treatment of cases of vitiligo on the service of Dr. Arnault Tzanck at the Hospital St. Louis in Paris.

*Ammi Majus Linn* is a yearly umbelliferous plant closely related to the plant *Ammi Visnaga*, from which it can be differentiated only with difficulty with the naked eye. *Ammi Majus Linn* is well known in Egypt where it is found abundantly in the Nile delta, but it has also been grown in French soil. Since the 13th century the Egyptians have used a powder prepared from the fruit of this plant for the treatment of leukoderma. However, the powder of *Ammi Majus Linn*, just like that of *Ammi Visnaga*, provoked such undesirable manifestations as headache, nausea, vomiting, diarrhea, gastric burning and, when given in very strong doses, even nephritis and coma.

In 1947, I. H. Fahmy and H. Abu-Shady (1) undertook to extract the active principle of this plant. They were able to isolate two crystalline bitter substances, close to the furocoumarines, namely Ammoidin (C_{11}H_{16}O_{4} with a melting point of 148°) and Ammidin (melting point 98°). They also assayed the toxic dose on toads and found it to be 400 mg per kg weight for Ammoidin and 800 mg per kg weight for Ammidin.

EXPERIMENTAL

Experimentation with these substances was started in 1949 in Egypt by El Mofti, A. Abdel Malek and Hassan Hefnaoui (2). In April 1951, we began treatment with *Ammi Majus Linn*, in six patients with vitiligo, five men and one woman. Their ages were from 30 to 50 years. Three of these patients previously had been treated with various other procedures (arsenic, gold salts, oil of bergamot plus ultraviolet lamp light, p-aminobenzoic acid, vitamins B and C) without any noticeable effect.

Two of these patients presented lesions distributed over many parts of the body, while four presented less numerous areas which were principally located on the face, neck, forearms, and hands. Serologic tests for syphilis, determinations of the basal metabolic rate and blood counts were done in all patients before start of the treatment and failed to show abnormal results.

*Ammi Majus Linn* can be used (a) by oral administration, (b) by local topical application at the affected sites followed by sun or ultraviolet lamp exposure, or, (c) by a combination of (a) and (b). Three of our patients were subjected to the combined treatment, two only to topical treatment and one to treatment by mouth for 5 months and from then on to the combined treatment.

The local treatment consisted of light swabbing of the skin with an alcoholic solution containing Ammoidin 7½ mg and Ammidin 2½ mg per milliliter. It was carried out in our patients 2 or 3 times per week followed by ultraviolet lamp

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irradiation during the first weeks and then sun exposures when this became feasible in May. The length of exposure to the ultraviolet lamp was a suberythema dose as determined in every patient in preliminary tests; the usual starting dose was 2 to 3 minutes at 80 cm distance. The healthy adjoining zones were covered with a 10% alcoholic solution of p-aminobenzoic acid and did not participate in the reaction.

Despite these precautions all the patients, after the first exposures, developed in the irradiated zones bullous reactions of more or less severe but constant degree similar to burns. These burns were treated with boric acid compresses and Dalibour cream, and after 10 days we were able to resume the local treatment.

![Fig. 1. Vitiligo of 15 years' duration, previously treated with many different procedure without any benefit. Treatment with Ammi Majus Linn by external application and by mouth produced a minimal result during the first two months and from then on a quicker and more significant improvement. On the body the plaques are in the process of repigmentation, except for the serotum where the vitiligo areas have not changed.](image)

The internal treatment consisted of ingestion of tablets containing Ammoidin 10 mg and Ammidin 5 mg starting with 1 tablet per day and gradually increasing to 4 tablets daily at the end of two weeks, if there were no signs of intolerance. The daily dose of 4 tablets was exceeded only in one of our patients.

Two of the four patients who received the internal treatment complained of nervousness and insomnia, and one of these also had nausea and gastric burning. In these patients the medication was interrupted for 8 days and was then resumed and was well tolerated: In one patient the weaker dose of 2 tablets per day and in the other patient 4 tablets per day on 2 out of every 3 days. One of the four patients even stated that there was an improvement in his general condition. Blood counts done after the treatment were normal.

In two of the three patients who received the combined treatment strongly pigmented islands with a follicle opening in the center appeared in the leukodermic plaques 21 days after start of the treatment (Figs. 1 and 2). In the third patient, the first areas of pigmentation were not seen until after 3 months.

In the two patients who received the local treatment only, the first areas of
pigmentation appeared 15 days after healing of the burns i.e., about a month after the start of the treatment. In distinction to the patients described above, only the areas to which the solution had been applied became repigmented.

Finally the sixth patient, who took 4 to 6 tablets per day for 5 months (i.e., since March) without any side effects but also without any evidence of repigmentation, noticed a sudden start of repigmentation in August after only two local applications with subsequent exposure to the sun (Fig. 3). Although not all the plaques were exposed to the sun and though the sun exposures were entirely interrupted for one month, the repigmentation has become generalized and has progressed rapidly.
In three of our patients, a generalized pruritus in all the plaques preceded the onset of the repigmentation.

**DISCUSSION**

The repigmentation appeared in all patients as pigmented minute macules with hair follicles in their center. These macules were distributed over the leukodermic plaques and increased progressively in size until they joined, forming larger islands. This was particularly distinct in the lesions on the trunk and on the extremities. On the face the repigmentation developed more rapidly and appeared to be progressing more from the periphery towards the center. Some of our patients, who have now been under treatment for 5 months and in whom the face is entirely repigmented, still present on the trunk, the legs and especially
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on the feet, plaques which merely show spotty repigmentation. The areas of vitiligo which have developed most recently appear to be the ones which respond best to treatment. As a matter of fact, the genital region which, in some, was the first region to become involved has not responded to this treatment in any of our patients.

The repigmentation does not seem to occur simultaneously in all the plaques of vitiligo; rather, we have seen it to develop successively in different body regions but usually simultaneously in symmetrical regions of the body. The newly pigmented sites are always significantly darker in color than in the normal surrounding skin. But this hyperpigmentation fades out very quickly, and then the previously depigmented skin takes on the same color as the surrounding skin. In the hairy areas the appearance of repigmentation of the skin is preceded by restoration of the hair pigment. Repigmentation appeared in the same manner in the areas which had a vesicular reaction after sun or ultraviolet exposure as in those which did not, indicating that vesiculation is not a prerequisite for production of the pigment. The sun also appears to have a more significant effect than the ultraviolet lamp.

Is there an effect from the internal administration of Ammi Majus Linn? It is very likely, for in the patients who had received internal treatment we have seen the same islands of repigmentation appear in the plaques which had not received local treatment as in those which had. Moreover, certain patients have told us that the ingestion of the tablets alone, without local application of the solution, provoked a marked erythema of the lesions after exposure to the sun; even the normal skin, after internal treatment, seemed to become much more pigmented after sun exposure than previously and tended to develop more than the usual degree of sunburn. Also the rapid repigmentation in 3 days after 2 sun exposures, in the patient who had first had 5 months’ internal therapy, would indicate the efficacy of the internal treatment.

Thus it appears that the plant Ammi Majus Linn has a specific action in vitiligo; the similarity of the response of the 6 patients cannot be explained as a chance finding. However, this investigation has been carried out in too small a number of patients to permit the drawing of final conclusions. It is well to remember that none of our patients is as yet completely cured in all affected areas and that one cannot foretell whether there will be any recurrences. Two of our patients who still are under treatment and whose lesions are in the process of repigmentation, nevertheless have shown some new areas of vitiligo. The mechanism of action of Ammi Majus Linn must still be investigated. In any event the first results which we have observed are sufficiently impressive to make us continue our studies.

REFERENCES