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USE OF TOLBUTAMIDE IN THE TREATMENT OF ACNE

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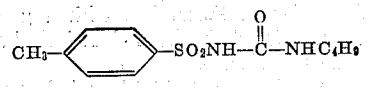
This invention relates to an improved method in the treatment of acne particularly pustular acne and more particularly to the treatment of acne by means of an orally ingested drug, tolbutamide.

The treatment of acne is not a simple "magic bullet" affair. In severe cases of acute pustular acne, local therapy alone is of little value. The specific systemic measures usually employed in addition to local therapy depend upon the seriousness of the skin condition. Additional measures which have been used in the past include: hormone therapy, particularly diethylstilboestrol; dietary control; vitamin supplements, particularly vitamin A and vitamin C; ultra-violet and X-ray therapy; administration of toxoids and vaccines; and use of antibiotics, such as sulfonamides; penicillin, erythromycin chloramphenicol, oleandomycin tetracycline and novobiocin. Isoniazid has also been used. Most consistent results have been achieved with chloramphenicol and erythromycin. Nevertheless treatment with antibiotics is unsatisfactory since, while a favourable response is usually obtained, this is followed by a new flare-up, and relapses are frequent after discontinuance of the antibiotics. The other forms of drug therapy are also not completely effective.

It is an object of the present invention to provide an improved therapy for the relief of symptoms of acne.

This object is achieved in the method of treating acne which comprises: selecting a human having acne; and feeding said human a therapeutically effective dose of tolbutamide.

Tolbutamide, i.e. a sulfonamide having the formula



has been used in the treatment of diabetes mellitus. However it has now been discovered that tolbutamide has unexpected utility in the treatment of acne, since tolbutamide has no bactericidal effect.

Usually, the therapy consists in the ingestion, by the patient suffering from acne, of tablets containing tolbutamide. Usually a maximum of about 1 gram of tolbutamide per day is given since otherwise there is an undesirable hypoglycemic response in non-diabetic patients suffering from acne. Thus, in dosages of 1.0 gram tolbutamide, blood sugar levels are lowered about 10% in normal individuals.

A convenient form of treatment is the use of tablets containing from 0.250 to 1.0 gm. tolbutamide, an especially convenient amount being 0.5 gram tolbutamide per tablet. Preparation of such tablets will be described hereinafter.

A series of patients were treated for acne with tolbutamide according to the method of the present invention. Some patients had deep pustular acne, chronic staphyloderma, recurrent furunculosis, sycosis vulgaris, hidradenitis suppurativa or hidrosadenitis axillaris, and other resistant pustular infections of the skin.

Only patients who were resistant to therapy by the usual methods of treatment were treated according to the present invention. They were instructed to continue taking carbohydrates in their diet, including candy and fruit if desired. All those patients with severe acne received a tablet containing 0.5 gram tolbutamide every twelve hours, while those patients with milder cases of acne received one tablet containing 0.5 gram tolbutamide once a day.

The patients were seen at regular intervals and their blood sugars were determined at frequent intervals. The results of the blood sugar tests were always within normal limits.

The results obtained for the treatment of acne with tolbutamide according to the present invention is summarized below in Table I:

Table I

Case No.	Diagnosis	Prior Treatment	Results after treatment with tolbutamide (Time results achieved), months		
			Fair	Good	Excellent
1	Pustular acne	Antibiotics, X-ray and local therapy		2	
2	do	X-ray and local therapy		1½	
3	Hidradenitis suppurativa	Antibiotics, X-ray and local therapy	3		
4	Severe pustular acne vulgaris	Antibiotics, X-ray therapy		3	
5	Papulo-pustular acne vulgaris	X-ray and local therapy			4
6	Sycosis barbae vulgaris, pustular lesions	Antibiotics, X-ray therapy		1	
7	Acne vulgaris	X-ray and local therapy			1
8	Pustular sycosis barbae	X-ray, local therapy, antibiotics		2	
9	Very severe pustular acne	X-ray therapy, local treatment			4
10	Deep pustular acne	Antibiotics, X-ray and local therapy		2	
11	Cystic, pustular acne vulgaris	X-ray and local therapy			2
12	Severe pustular acne vulgaris	do		2	
13	Papulo-pustular acne vulgaris	X-ray therapy		3	
14	Deep pustular acne	X-ray, local therapy, antibiotics			3
15	Papulo-pustular acne vulgaris	do		2	
16	do	X-ray and local therapy			1
17	Severe pustular acne vulgaris	X-ray therapy and antibiotics	3		
18	Rosacea with acneiform lesions	Antibiotics, local and X-ray therapy			2
19	Pustular acne vulgaris	X-ray and local therapy	1		
20	do	do	(1)	(1)	(1)
21	Acne rosacea	X-ray therapy and antibiotics		2	
22	Severe pustular acne	do	3		
23	Deep pustular acne	do			4
24	Acne rosacea with deep acneiform lesions and moderate rhinophyma.	X-ray and local therapy, antibiotics		4	
25	Sycosis barbae vulgaris	X-ray therapy and antibiotics		3	
26	Pustular acne vulgaris	X-ray therapy	2		

[1] Nausea and diarrhoea.

It is seen from the above table that all patients experienced improvement following treatment with tolbutamide according to t e teachings of the present invention. No hypoglycemic reactions were observed.

The following case reports are intended to describe more completely the beneficial results following treatment with tolbutamide following the teachings of the present invention.

Case 3.—Mrs. M. C. (practical nurse), aged 50, with a long history of recurrent furunculosis involving groin, external genitalia, breast and nipple areas, was treated by incision and drainage and X-ray therapy, and was allergic to many antibiotics except oleandomycin and erythromycin. She had many recurrent flare-ups. She was first seen with subcutaneous nodular, painful lesions, involving groin and perianal and vulvar regions, as well as a few in the axillae. Some were soft and fluctuating and discharged purulent material which on culture grew a haemolytic staphylococcus. The diagnosis was: hidradenitis suppurativa, or deep infection of the apocrine glands. Treatment included more X-ray therapy, ultraviolet light, antiseptic compresses and applications, tin oxide tablets, oestrogenic hormone, staphylococcus toxoid, and multiple vaccine therapy. She responded very well to erythromycin and oleandomycin, but with flare-ups of painful and recurrent furuncular lesions. The fasting blood sugar was 95 mg. percent and she had no glycosuria. She was then started on tolbutamide, 0.5 g., twice a day, and gradually showed a marked improvement with only occasional recurrences. The subcutaneous nodules did not develop into abscesses and underwent resolution. She is taking one tolbutamide tablet daily.

Case 4.—Mr. H. D., aged 20 (farmer), was first seen with a very severe and deep cystic and papulo-pustular acne vulgaris, and an associated oily seborrhoea. Face and forehead were covered with reddened cystic and deep acne pustular lesions, and many indurated papules. Some cysts were the size of a hazel nut and one was the size of a small walnut. He had been under the care of dermatologists for four years, and received much X-ray and local therapy.

He was then given more unfiltered X-ray therapy, Vleminckx's compresses, detergent soaps, staphylococcus toxoid, sulphur and resorcin cream and lotion, and a variety of antibiotics from sulfonamides to all the "mycins," responding best to chloramphenicol. There were many remissions and relapses. All therapy was stopped except local therapy and he was started on tolbutamide, 0.5 g. twice a day. He was instructed to take a little extra candy each day, and was given CO_2 therapy with acetone locally twice weekly. The response was sudden and dramatic. In two weeks, all pustular elements of the lesions disappeared. The active lesions subsided markedly and no new lesions appeared. He is being treated now for the late sequelae, and a few very superificial pustules still make their appearance. He is taking one tolbutamide tablet daily.

Case 9.—Mr. D. I. (mechanic), aged 22, had been treated for acne for five years at other centres and had received about 1000 r. of X-ray therapy. He was first seen presenting a deep cystic type of acne vulgaris of the face, shoulders and back, with innumerable sebaceous cysts and comedones and deep acne papulo-pustules. The reddened cysts were the size of a hazel nut, and the neck was involved with band-like keloidal lesions. He felt very insecure and afraid to face the public, and required tranquillizers. This patient had been treated by us by all known methods of acne therapy, including diet, Vleminckx's packs, resorcin, and sulphur lotions, stilboestrol and most of the antibiotics. He responded to acne surgery and chloramphenicol, injections of staphylococcal toxoid, vitamins, and ultraviolet light, but with relapses. He was then given tolbutamide, 0.5 g., twice daily. He began to show very marked and continued improvement. The purulent lesions diminished gradually

until no evidence of pyoderma was seen, but only acne sequelae with scarring.

Case 22.—Mr. J. H., aged 22 (school teacher), whose acne began at age 15, presented himself to us with a severe deep papulo-pustular acne vulgaris covering the entire back, face, shoulders and chest, with scarring and sequelae. Clinically, this was a case of acne aggregata seu conglobata. Many double comedones with severe perifollicular infection and confluent infiltration, and softening of the lesions with suppuration were present, lesions varying in size from a filbert nut to a marble and requiring many incisions and drainages. Under the care of another dermatologist for 3–4 years previously, he had received maximum doses of X-ray therapy to face, chest and back.

He was also given an acne diet and Vleminckx's packs, resorcin and sulphur lotions, stilboestrol, nearly all known antibiotics, injections of toxoid, and ultraviolet light, and all foci of infection were searched for. He would improve in the summertime with exposure to sunlight, but relapse in the winter with severe and deep pustular lesions. The patient was then given CO_2 therapy to the face and ultraviolet light to the body, injections of multiple vitamins, and one tolbutamide tablet, 0.5 g. twice a day, with a decided and marked improvement of all pustular elements. Local therapy was continued. A few lesions recurred when the patient could not afford medication, but when tolbutamide tablets were supplied to him the lesions gradually subsided. He is now taking one tolbutamide tablet daily with a dramatic subsidence of all lesions, except for the sequelae. Tolbutamide tablets will be stopped when no new lesions appear.

Case 27.—Mrs. M. N. (a stenographer) had been treated for pyoderma faciale, consisting of intense reddish cyanotic erythema associated with superficial and deep abscesses and cystic lesions. Some cysts were connected with communicating channels and sinus tracts with deep-seated pustular and linear scarring. Previous treatment consisted of incision and drainage, X-ray therapy, local therapy, injections of penicillin, sulfonamides, many antibiotics including chloramphenicol, ultraviolet light, CO_2 therapy, vitamins, staphylococcal toxoid, and vitamin D_2 and a search had been made for foci of infection. She had many remissions and relapses with pustular flare-ups. She was then given tolbutamide, with a gradual clearance of all pustular lesions. All lesions have cleared except the late sequelae.

Case 28.—Mr. J. L., age 29 (druggist), was first seen with a severe papulo-pustular acne vulgaris of face and neck and acne keloidal lesions of the back, deep-seated pustules and many cystic pustular lesions. He also had sycosis vulgaris. This patient had been under the care of other clinicians including dermatologists for many years, receiving X-ray therapy to the limit of tolerance. Under our care he was given acne surgery, ultra-violet light, CO_2, staphylococcus toxoid and all forms of local therapy, resorcin and sulphur lotion, vitamins A and C, isoniazid, stilboestrol, and a large number of antibiotics, with relapses and remissions. He was then started on tolbutamidle 0.5 g. twice daily, with a continued clearance of the lesions. He is still taking one tablet daily, and the lesions have cleared, only an occasional one reappearing. He is now being treated for the last sequelae.

The following example is given to show the preparation of a dosage unit form composition for use in the present invention.

Example 1: Tablets.—12.5 gms. of tolbutamide was thoroughly mixed with .25 gm. orange coloured starch. The mixture was then granulated with a small amount of 24% aqueous solution of gelatin and acacia containing 0.00625 gram of D and C Orange #4, 13.75 grams of orange coloured starch, 7.75 grams sodium bicarbonate and 2.0 grams magnesium stearate were then added. The mixture was then compressed into pellets, each weighing 620 mg.

The proportions used are sufficient to produce 25 tablets, each containing 0.5 gm. tolbutamide.

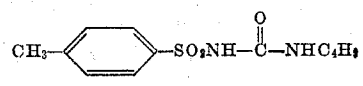
Example 2: Capsules.—Capsules containing 500 mg. of tolbutamide were prepared by mixing 500 mg. tolbutamide with 10 mg. of light mineral oil, and filled into hard gelatin capsules.

While the above examples show the tolbutamide being in admixture with starch as the diluent, other well-known diluents may also, of course be used. Also dosage unit forms other tablets, for example capsules, may be used.

In summary, therefore, the present invention provides an adjuvant in the treatment of acne. It has been found that the effects on acne (pustular) are usually better than those of the broad-spectrum antibiotics. In most patients good or excellent results were achieved.

What I claim is:

1. The method of treating acne which comprises the steps of (1) selecting a human afflicted with acne, and (2) feeding said human a therapeutically effective dose of a sulfonamide having the structure:



2. The method of claim 1 wherein the maximum daily dose of the sulfonamide fed is about 3 gms.

3. The method of claim 1 wherein the sulfonamide is fed in a dosage unit form containing about 0.5 gram of said sulfonamide.

4. The method of claim 3 wherein the sulfonamide is fed in tablet form.

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