

# EFFECT OF AZELAIC ACID ON SEBUM EXCRETION RATE: A COMPARATIVE STUDY BETWEEN TWO SAMPLING TECHNIQUES

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## ABSTRACT

In this study the influence of azelaic acid (AZA) 20% cream on the sebum excretion rate (SER) of 80 volunteers having mild to moderate acne vulgaris was demonstrated. Absorbent paper and Sebutape were used to collect the sebum and quantification was carried out by direct gravimetric method. It was shown that topical application of AZA creams could reduce the SER and number of acneic lesions as well as the grade of acne. Sebutape has the advantage of simplicity and reproducibility and direct weighing of Sebutape is preferred to the classic scoring method. A near correlation was observed between the two sampling methods, i.e., absorbent paper and Sebutape.

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**Keywords:** Azelaic acid, Sebum excretion rate, Acne, Sebutape

## INTRODUCTION

Azelaic acid (AZA) is a naturally occurring straight-chained saturated dicarboxylic acid. It is a competitive inhibitor of tyrosinase<sup>1</sup> and has a cytotoxic effect on human malignant melanocytes.<sup>2,3</sup>

Following topical application of AZA in various skin disorders, a significant improvement of acne lesions has been observed. Treating acne with AZA cream has been reported in acneic patients without chloasma.<sup>4,5</sup> Furthermore, it was shown that AZA has a marked effect in reduction of cutaneous micrococcae and propionibacterium sp. without modification of the sebum excretion rate (SER).<sup>6</sup>

Topical AZA demonstrated comparable anti-acne efficacy to topical tretinoin, benzoyl peroxide, erythromycin and oral tetracycline.<sup>7</sup> AZA is well tolerated and with limited adverse effects.<sup>7</sup> It is non-teratogenic, is not associated with systemic side-effects and does not induce

resistance in *P. acnei*.<sup>8</sup>

The gravimetry method for quantification of SER has been widely employed.<sup>9,10</sup> A more direct method was also reported<sup>11</sup> in which the collecting papers were pre- and post-weighed under defined conditions of temperature and relative humidity.

By introducing "Sebutape" in 1986, the visualization of individual sebum droplets and determination of SER became possible.<sup>12,13</sup> In the present study, the influence of topical AZA on SER has been demonstrated. The quantification of SER in both sampling techniques was carried out by gravimetric method.

## MATERIAL AND METHODS

Sebutape (Cu Derm Corp., Texas) and absorbent papers (General Papers & Box Company, Pontypridd, UK) were used. Azelaic acid 20% cream (Schering, Berlin) was purchased from the market. Eighty volunteers (49 males

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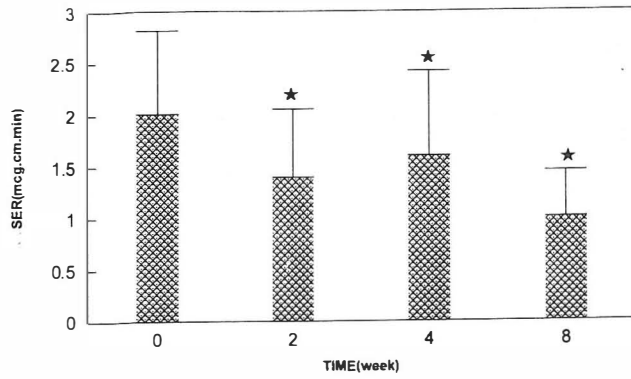


Fig. 1. The effect of AZA on reduction of SER during eight weeks of treatment. \* $p < 0.001$ .

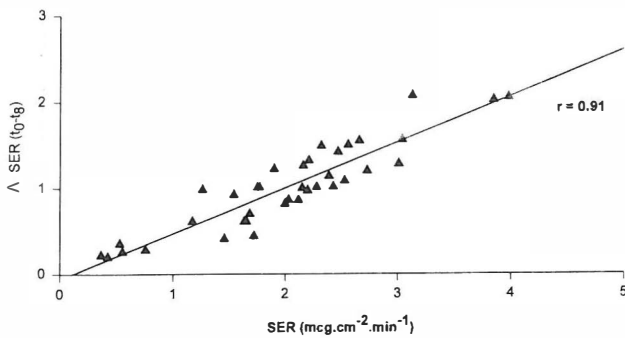


Fig. 2. Correlation between baseline SER and the variation of SER before and after treatment.

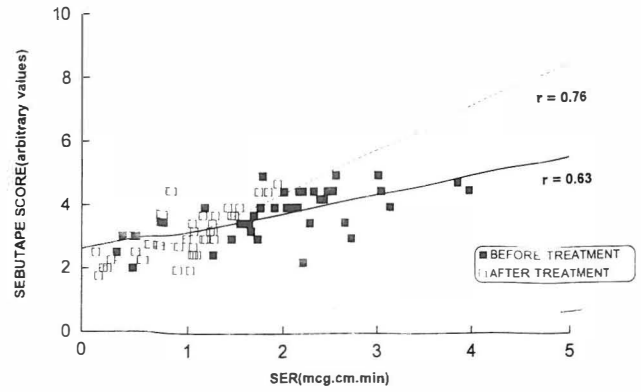


Fig. 3. Correlation between SER ( $\text{mcg.cm}^2.\text{min}^{-1}$ ) and Sebutape score for eight weeks of treatment with AZA.  $p < 0.001$ .

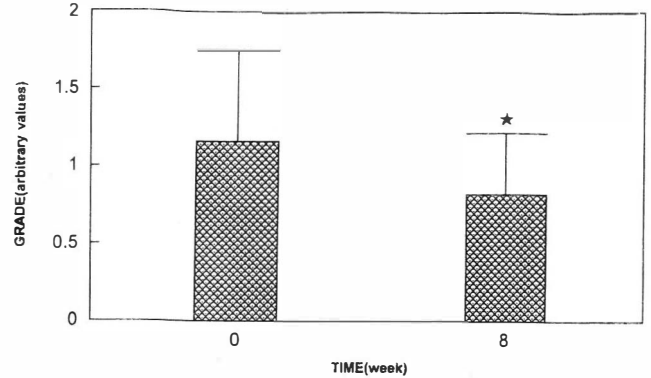


Fig. 4. The effect of AZA on total acne grade after eight weeks. \* $p < 0.001$ .

and 31 females) aged 20-30 years (mean  $24.5 \pm 5.5$ ) who had moderate acne vulgaris participated in the study. The volunteers gave written informed consent after receiving detailed instructions concerning the study performance, restrictions, and possible adverse effects. Volunteers were not allowed to take any medication from one month prior to the study. All recordings were performed in December and January over two consecutive days in the afternoon between 1 and 4 pm. The patients washed their hair on the evening prior to sebum collection with a mild shampoo and were not permitted to apply any topicals to the scalp or forehead. The females were not on their menstrual cycle before treatment with AZA.

Before treatment, clinical assessments were made by grading the acne and counting the total lesions of the face according to a well-performed technique proposed by Burke and Cunliffe.<sup>14</sup>

The forehead was degreased by washing with a mild soap. The remaining lipids were removed with cotton wool gauze soaked in 70% ethanol followed by rinsing and drying with mild tissue. Two sheets of absorbent paper with  $8.75 \text{ cm}^2$  area ( $2.5 \times 3.5 \text{ cm}$  each) were placed onto the forehead, covered with gauze, and kept in position by a broad rubber band. Measurement of SER was carried out by direct gravimetric method.<sup>13</sup>

With a one day interval, the Sebutapes were applied on the right and left zones of the forehead of the same patients. Evaluation of SER by Sebutape was performed using two Sebutapes of  $3.8 \text{ cm}^2$  area, preweighed and symmetrically placed on the forehead. The tapes were removed after 1 h and two new tapes were re-applied. The procedure was repeated for 3 h. The quantification of SER was carried out by gravimetry and the number and size of holes were visually scored according to the manufacturer's reference patterns. Azelaic acid cream was applied twice daily and modifications of SER, amelioration of lesion, etc. were considered during the treatment.

A computer program (SPSS/PC ver 4 for DOS) was used for statistical interpretation of results.

## RESULTS

Statistical analysis of results with paired t-test showed a significant reduction of SER after treatment with AZA. The difference between the 2nd and 4th week was not statistically significant ( $p < 0.001$ ) (Fig. 1).

The efficacy of the drug (variation of SER before and after treatment) was not related to sex, but a close correlation with baseline SER was observed ( $r = 0.91$ ,  $p < 0.001$ ). The

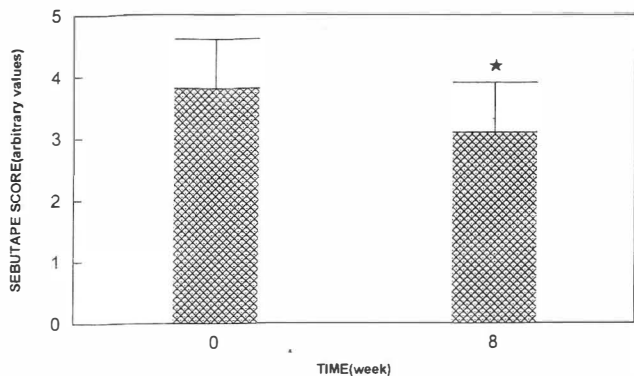


Fig. 5. The effect of AZA on Sebuptape score after eight weeks. \* $p < 0.001$ .

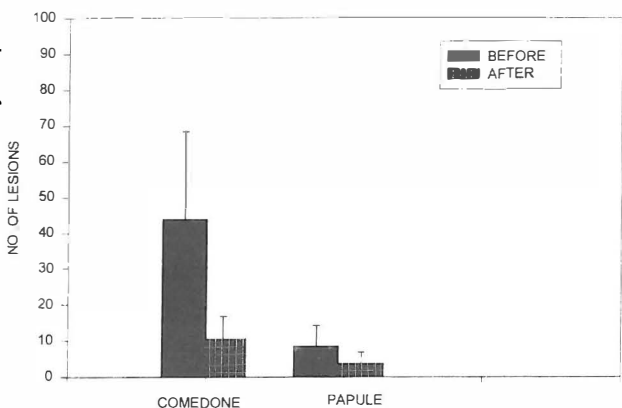


Fig. 6. Changes in number of acne lesions (mean  $\pm$  SD) treated with topical AZA over eight weeks.  $p < 0.001$ .

patients having high SERs were more sensitive to treatment with AZA (Fig. 2).

Fig. 3 indicates the score measurement of the baseline sebum level of the skin versus SER values in the same patients ( $r = 0.76, p < 0.001$ ). Azelaic acid could significantly reduce the grade of acne lesions (Fig. 4) and this reduction was related to SER.

A significant reduction in Sebuptape score measurement was demonstrated after 8 weeks of treatment (Fig. 5). A significant decrease in total lesion counts was also observed after 8 weeks of treatment. The reduction was significantly lower in comedones as compared to inflamed lesions (Fig. 6).

A high correlation was found between grade of acne and number of inflamed lesions (Fig. 7), but there was no correlation between acne grade and the number of comedones.

Table I summarizes the SER of 80 patients measured by gravimetry using Sebuptape and absorbent paper.

Direct gravimetry of absorbent paper has been done at  $60 \pm 5\%$  RH. The variation of RH could significantly modify the results of the gravimetric method. The coefficient of variation (C.V.) will increase two-fold by increasing the

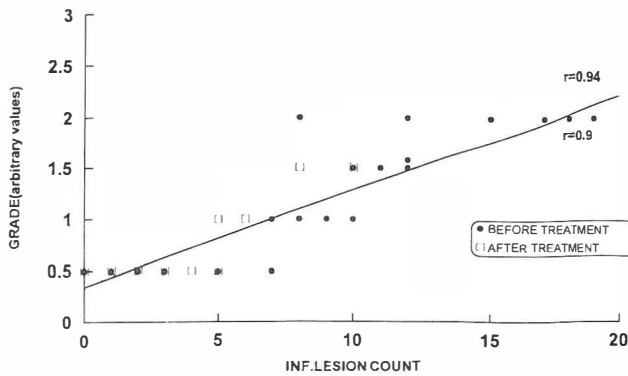


Fig. 7. The effect of inflamed lesion counts on total acne grade.  $p < 0.001$ .

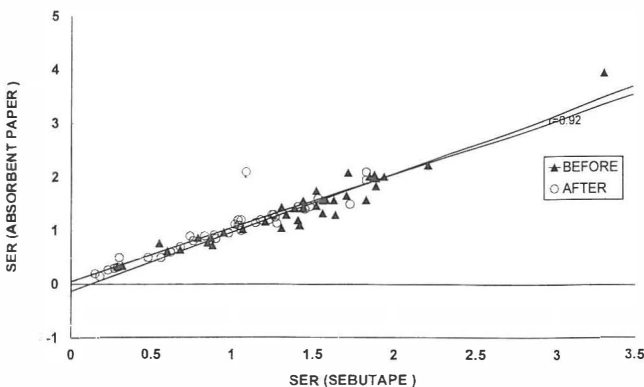


Fig. 8. Correlation between SER ( $\text{mcg.cm}^{-2}.\text{min}^{-1}$ ) values obtained from gravimetry method (Sebuptape absorbent paper) before and after eight weeks of treatment.  $p < 0.001$ .

relative humidity (RH) from 60 to 80% with Sebuptape, while the variation of SER was not significantly affected by a change in RH.

## DISCUSSION

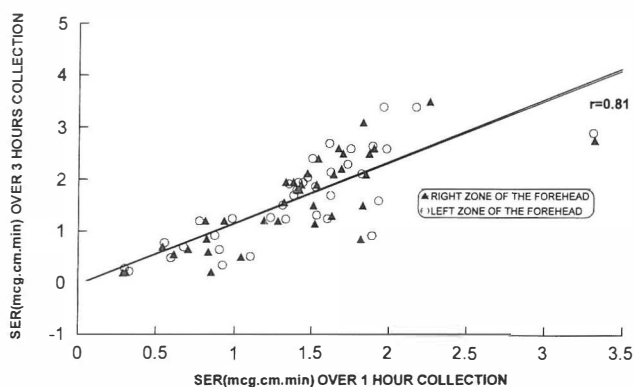
Azelaic acid has been reported to be of value in the treatment of mild to moderate acne vulgaris. This acid presents enormous advantage and very low side-effects. Some publications indicated the inefficacy of AZA in reduction of SER after 6 weeks of treatment.<sup>15</sup> We have demonstrated that application of AZA 20% cream for 8 weeks could reduce the SER in patients with moderate acne. It was shown that the the number of acneic lesions, grade of acne and Sebuptape score were markedly reduced following topical application of AZA.

The technique of sampling is also important in the evaluation of SER. A simplified gravimetric method by pre- and post-weighing of collecting paper was proposed<sup>14</sup> in order to eliminate the disadvantages of solvent extraction.

Our experimentation indicated that direct gravimetry of absorbent paper remains reliable, with some disadvantages.

Table I. Sebutape and absorbent paper gravimetry recordings (mean±S.D.) of 80 patients 1,2 and 3h after degreasing.

Recording	Time after degreasing (h)		
	1	2	3
Sebutape:			
SER (mcg.cm <sup>-2</sup> min <sup>-1</sup> )	2.25±0.9	2.42±0.7	1.34±0.21
C.V.	40%	28.92%	15.67%
Score	—	—	3.81±0.79
Absorbent paper:			
SER (mcg.cm <sup>-2</sup> min <sup>-1</sup> )	2.21±1.22	2.45±0.8	1.34±0.72
C.V.	55.20%	32.65%	53.73%

Fig. 9. Correlation between SER(mcg.cm<sup>-2</sup>.min<sup>-1</sup>) values obtained at 1 hour and 3 hours of collection.  $p < 0.001$ .

The weight of papers changed with variations in ambient temperature and relative humidity. Weighing should only be carried out at defined conditions of temperature and RH.

In contrast, Sebutape is a hydrophobic polymer film which permits the selective passage of skin lipids; corneocytes and other non-sebum factors are absent in microscopic study of Sebutape. For quantitation of SER we suggest replacing classic Sebutape scoring by direct gravimetry which is more precise and reproducible. The correlation of SER evaluation by two sampling methods is given in Fig. 8.

A significant correlation was observed between SER values obtained over 1 and over 3 h on the left and right sides of the forehead (Fig. 9).

Therefore, SER can be measured in humans 1 h after defatting, without noticeable loss of accuracy.

Considering the safety, reduced allergic sensitization and less cutaneous irritation in comparison with topical benzoyl peroxide and tretinoin,<sup>16</sup> and regarding the present findings, one can assume that AZA is another option for topical treatment of mild to moderate inflammatory acne vulgaris.

Finally, it is important to note that a twice daily application of AZA cream for 8 weeks seems to be necessary in order to ameliorate acne and to reduce the SER.

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