

Impact of Solanum Melongena Peel on Arsenic-Induced Bowen's Disease

Razia Sultana¹, Tasaduk Kabir², M Azizul Haq³, Murtoza Shahriar⁴, Nigar Jahan Sonia⁵, Simonto Mirza⁶, Nakib Kamran Oni⁷

¹ Assistant professor, Department of Pharmacology, Monowara Sikder Medical College

² M.S Student, Bangladesh Agricultural University, Bangladesh

³ Medical officer, ENT Care Center, Gulshan, Dhaka

⁴ Resident Medical officer, Feni Cardiac Centre and Specialised Hospital

⁵ Assistant professor, Department of Biochemistry, Marks Medical College and Hospital

⁶ M.S Student, Department of Physical and Mathematical Sciences, Chattogram Veterinary and Animal Sciences University

⁷ Senior House officer, Emergency Department Barking, Havering and redbridge University Hospitals, NHS Trust

ABSTRACT

Background with objective: About millions of Bangladeshi people are chronically exposed to high concentration of arsenic through contaminated drinking water and thus suffering from arsenic-related health hazards. In arsenicosis, skin manifestations like melanosis, leucomelanosis and keratosis occur commonly. In addition, it may cause Bowen's disease. This study was conducted to confirm the effect of the ointment containing *Solanum melongena* peel extract in the treatment of arsenic-induced Bowen's disease.

Methodology: This Observational comparative study was carried out among 08 arsenic induced Bowen's disease patients at the Pharmacology department, Bangladesh Medical University (BMU), Dhaka and two arsenic affected endemic areas [Bhanga Upazilla of Faridpur District (about 150 km from Dhaka) and Babutipara Union, Muradnagar Upazilla, Cumilla District (about 108 km from Dhaka)] from September 2017 to January 2019. Purposive sampling was done according to availability of the patients. All the data were compiled and sorted properly and the quantitative data was analyzed statistically by using Statistical Package for Social Science.

Result: In patients with arsenic-induced Bowen's disease, the mean ($\pm$ SD) size of the lesions was 4.5 ± 2.9 cm² before intervention and 2.7 ± 1.9 cm² after interventions. The percentage of reduction was 40. P-value was 0.027 for arsenic-induced Bowen's disease. This result was statistically significant.

Conclusion: The present study reveals that *S. melongena* peel extract is effective in the treatment of clinically diagnosed, arsenic-induced Bowen's disease.

KEYWORDS: Solanum melongena peel, Bowen's disease, Arsenic

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INTRODUCTION

Bowen's disease (intraepithelial carcinoma or carcinoma *in situ*), Squamous cell carcinoma and basal cell carcinoma are common malignancies found in patients with long-term exposure to arsenic. Arsenic-related Bowen's disease can appear 10 years after arsenic exposure, while other types of skin cancer can have a latency period of 20 or 30 years¹. Bowen's disease usually appears as a slowly enlarging, erythematous, well-demarcated patch or plaque and has a scaling or crusted surface. It occurs as a solitary lesion, but the number may be several and has 3-5% risk to develop squamous cell carcinoma². Treatment options available for

Bowen's disease include cryotherapy^{3,4}, curettage and cautery^{5,6}, topical 5-fluorouracil^{7,8}, acitretin⁹, 5% imiquimod¹⁰, photodynamic therapy and excision². Topical 5-fluorouracil may cause widespread dermatitis and painful erosion⁷, whereas, 5% imiquimod sometimes cause significant erythema and crusting¹⁰. However, these treatments are expensive and moderately painful, have chance of slow healing and scarring and also need specialized training of health professionals with appropriate facilities¹¹. *Solanum melongena* L. (brinjal/eggplant) belongs to the genus Solanaceae, is a common vegetable in Bangladesh. Both fruit and peel of *S. melongena* contain

Impact of Solanum Melongena Peel on Arsenic-Induced Bowen's Disease

solasodine alkaloid which showed anti-cancer property¹². *S. melongena* peels were reported to possess antioxidant activity as it contains anthocyanin, delphinidine-3-(p-cumaroylrutinoside)-5-glucoside (nasunin)^{13,14}. Delphinidine, a flavonoid pigment, has an inhibitory effect on human fibrosarcoma HT-1080 invasiveness *in vitro*¹⁵. A skin cream containing a constant mixture of SRG (solasodine rhamnosyl glycosides) consisting of solasodine containing triglycosides solasonine (β -solatriose 33%), solamargine (β -chacotriose 33%) and di and monoglycoside (34%) was found effective in the treatment of keratosis (non-arsenic origin), squamous cell carcinoma and basal cell carcinoma¹⁶. One study conducted to evaluate the effect of *S. melongena* peel extract in the treatment of arsenic-induced Bowen's disease.

MATERIALS & METHOD

This Observational comparative study was carried out among 08 arsenic induced Bowen's disease patients at the Pharmacology department, Bangladesh Medical University (BMU), Dhaka and two arsenic affected endemic areas [Bhanga Upazilla of Faridpur District (about 150 km from Dhaka) and Babutipara Union, Muradnagar Upazilla, Cumilla District (about 108 km from Dhaka)] from September 2017 to January 2019. Purposive sampling was done according to availability of the patients. Ethical clearance for the study was obtained from the Institutional Review Board of Bangladesh Medical University. Written informed consent (Bangla version) was taken from every patient. All data were collected through a pre-structured questionnaire. After collection of data, they were checked for errors and then analyzed using the statistical software SPSS 25. All the patients were demonstrated how to apply the ointment containing extract at the lesion site. The clinical examination of patient and distribution of ointment containing *S. melongena* peel extract were done at 2 weeks interval. Detailed history, clinical examination, and photographs of the lesions were collected. The size of the lesions was measured before and after completion of the study. Drinking water and nail samples were collected for estimation of arsenic. One labeled polyethylene container (capacity 100 mL) containing 1 drop of nitric acid was supplied to each patient in order to collect the water sample. All the collected samples were then transported to the Department of Pharmacology, Bangabandhu Sheikh Mujib Medical University and stored until analysis. A labeled, sterile, air-tight, polyethylene bag was supplied to each patient and advised to collect finger and toe nails (growth of one month). About 200-500 mg nail samples of each patient were collected and transported to the laboratory and stored in the refrigerator until analysis. The amount of arsenic in water and nails was measured by modified silver diethyldithiocarbamate (SDDC) method. Specific species of *S. melongena* L was identified by Bangladesh National Herbarium. Then *S. melongena* was collected from the local

market. The average length of *S. melongena* were six to eight inches, circumference were three to four inches and weight was ranged from 200-300 g. *S. melongena* was rinsed thoroughly with water and dried off. Peels were removed with a peeler and cut into small pieces. Peels were then air dried at room temperature avoiding direct sunlight for two days. Dried peels were immersed into an amber color bottle containing one liter of the mixture of ethanol: chloroform: acetic acid (65: 32: 3) and kept for 72 hours at room temperature. After 72 hours, the peels and solvent were filtered through a filter paper. Filtered liquid was concentrated using a rotary evaporator at 40-50°C temperature.

BRINE SHRIMP LETHALITY STUDY

About three gram of brine shrimp (*Artemia salina*) eggs collected from the local market were poured into a glass tank (capacity = 6 L) containing artificial seawater (about 4 L) for hatching up to 48 hours with continuous aeration by air flow machine and artificial light using 60 watt bulb. One milligram extract of *S. melongena* peel was weighted by the electronic balance and dissolved in 1 mL of water to prepare the stock solution. Serial dilution of the stock solution was done and taken in four sterile, labeled test tubes. The concentration of the solutions after serial dilution was 100, 10, 1 and 0.1 µg/mL. The brine shrimp larvae (nauplii) were collected with a Pasteur pipette from the hatching chamber in the test tubes. Different concentrations of the extract were poured into the test tubes containing ten nauplii and kept in room temperature. Motility of the nauplii was observed after 2 and 24 hours. Percentage of death = $\left[\frac{\text{Number of dead nauplii}}{\text{Number of dead nauplii} + \text{Number of live nauplii}} \right] \times 100$. The ointment (100 g) contained 30 mg of *S. melongena* peel extract, 3.97 g stearyl alcohol, 10 g white wax and 86 g white petrolatum. White petrolatum, bee wax and stearyl alcohol were measured by an electronic balance after calibration and taken in a glass beaker. The glass beaker was placed into the bowl containing water and heated up to complete melting of the ingredients using Bunsen burner. After complete melting of the ingredients, the burner was put off and the beaker was placed in a tray for cool down. After reaching at room temperature, *S. melongena* peel extract was added and stirred well. Ointment was poured into the high-density polyethylene container and stored in a cool and dry place until supplying to the patient. The ointment was distributed and each patient was demonstrated separately how to apply the ointment at the lesion site. Patients were instructed to apply the ointment twice daily in the morning and bedtime for 13 weeks. An adherence sheet was provided to each patient and advised to put a tick mark at the appropriate place after applying the ointment. The keratotic lesion was monitored. Any improvement was documented and checks the adherence in every follow-up visit at two weeks interval. Paired t-test was

Impact of Solanum Melongena Peel on Arsenic-Induced Bowen's Disease

performed manually to measure the differences between the keratotic nodular size changes before and after treatment.

RESULTS

The mean ($\pm$ SD) age of the patients was 56.2 ± 4.4 years. The mean amount of arsenic in the tube well water

consumed by the patients was 222.4 ± 111.3 $\mu\text{g/L}$ and in the nail sample of the patients was 8.8 ± 4.3 $\mu\text{g/g}$. The mean duration of exposure to arsenic contaminated water of the patients was 11.3 ± 1.7 years. The mean duration of the appearance of lesions was 6.5 ± 2.1 years (**Table 1**).

Table 1: Characteristics of the patients (n=8)

Parameters	Arsenic-induced Bowen's disease (n = 8)
Male patients (n)	6
Female patients (n)	2
Age (years)	56.2 ± 4.4
Amount of arsenic in tube well water ($\mu\text{g/L}$)	222.4 ± 111.3
Amount of arsenic in nail ($\mu\text{g/g}$)	8.8 ± 4.3
Duration of arsenic exposure (years)	11.3 ± 1.7
Duration of appearance of symptoms (years)	6.5 ± 2.1

Data are presented as mean $\pm$ SD

In patients with arsenic-induced Bowen's disease, three patients were exposed to arsenic for about six to ten years and their reduction of the size of lesions was 60.3% and five patients were exposed to arsenic for about 11 to 15 years and their reduction of the size of lesions was 21.6% (**Table 2**).

Table 2: Distribution of patients according to the duration of arsenic exposure

Duration of arsenic exposure (years)	Arsenic-induced Bowen's disease (n = 8)	
	Number of patients	%Reduction
6 - 10	3	60.3
11 - 15	5	21.6

Impact of Solanum Melongena Peel on Arsenic-Induced Bowen's Disease

In patients with arsenic-induced Bowen's disease, two patients had skin lesions for about five years and their reduction of lesion size was 36.5%. Remaining six patients had skin lesion for about six to ten years and their reduction of lesion size was 37.2% (Table 3).

Table 3: Distribution of patients according to the duration of appearance of the lesions

Duration of the lesions (years)	Arsenic-induced Bowen's disease (n = 8)	
	Number of patients	%Reduction
1 - 5	2	36.5
6 - 10	6	37.2

In patients with arsenic-induced Bowen's disease, three patients had about 200 µg/ L arsenic in water and their reduction of lesion size was 68.2% and the amount of arsenic in water was within 200 - 400 µg/ L in remaining five patients and their reduction of lesion size 66.3% (Table 4).

Table 4: Distribution of patients according to the concentration of arsenic in water

Concentration of arsenic in water (µg/ L)	Arsenic-induced Bowen's disease (n = 8)	
	Number of patients	%Reduction
0 - 200	3	68.2
201 - 400	5	66.3

In patients with arsenic-induced Bowen's disease, the mean ($\pm$ SD) size of the lesions was 4.5 ± 2.9 cm² before intervention and the mean size was reduced to 2.7 ± 1.9 cm² after intervention. The percentage of reduction was 40. Statistical analysis was done by paired t-test and p-value was 0.027. The result was statistically significant (Table 5).

Table 5: Measurement of size of the lesion (cm²) before and after intervention

Arsenic-induced Bowen's disease (n = 8)		p-value
Before intervention	After intervention	
0.27	0.18	
2.8	2.6	

Impact of Solanum Melongena Peel on Arsenic-Induced Bowen's Disease

3.2	1.4	0.027
4.0	4.0	
6.7	1.8	
8.7	6.4	
8.1	3.9	
2.9	1.7	< 0.027*
4.5 ± 2.9	2.7 ± 1.9	

Data are presented as mean ± SD *Paired t-test

DISCUSSION

In the present study, reduction of the size of the skin lesions in patients with Bowen's disease was achieved after application of ointment containing *S. melongena peel* extract. The improvement was assessed clinically. In another study, Bowen's disease treated with diclofenac gel and hyaluronan gel ¹⁷ twice daily showed no residual disease clinically and histologically after 90 days in one patient but another patient discontinued treatment after 80 days due to development of severe dermatitis at the application site. A study conducted in two arsenic-induced Bowen's disease patients treated with acitretin 1 mg/kg orally for 10 months ⁹ showed improvement in one patient but another patient discontinued treatment due to systemic adverse effects. Acitretin is a retinoid analog act by inhibiting the excessive cell growth and keratinization. A study was conducted to evaluate the effect of *S. melongena peel* extract in the treatment of arsenic-induced Bowen's disease ¹⁸. Improvement was assessed by measuring the size of the lesions before treatment and after completion of treatment. A study was conducted ⁷ to compare photodynamic therapy and topical 5-fluorouracil in non-arsenic-induced Bowen's disease. During follow-up at 12 months, clinical clearance was 88% with recurrence in two patients in photodynamic therapy and 67% with recurrence in six patients in 5-fluorouracil group. 5-fluorouracil is a pyrimidine analogue that acts by interfering DNA synthesis and acts nonspecifically both in cancer and normal cells. Four patients developed widespread dermatitis and painful erosion during 5-fluorouracil therapy and discontinued treatment. There was no obvious adverse effects occur in photodynamic therapy except pain during initial treatment but the therapy is expensive. Topical 5% imiquimod cream was found effective in a retrospective study conducted in 2007 ¹⁰. In the study, complete clinical response was more than the present study but there was significant erythema

and crusting. Imiquimod is an immune response modifier which has anti-viral and anti-tumor effects.

CONCLUSION

The study suggest that ointment containing *S. melongena peel* extract is effective in reducing the size of the arsenical keratotic nodules as well as the lesions of clinically diagnosed, arsenic-induced Bowen's disease. Further extensive study should be done in a larger sample size.

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CONFLICT OF INTEREST

Authors declare no conflict of Interest.

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