SILVER SULFADIAZINE DRY FOAM-A NEW DELIVERY SYSTEM FOR PSEUDOMONAS BURN SEPSIS

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Of all the traumatic injuries, burns are one of the most horrendous experiences to human body characterised by high mortality and morbidity[1'7]. Silver sulfadiazine cream is the widely accepted form of topical therapy to control surface infection especially with *Pseudomonas aeruginosa*[3'4'5'6]. Application and removal of cream from the weeping wound is quite cumbersome and causes pain to the patient, Hence a topical dosage from, dry foam, has been formulated which can be easily appled to the denuded area of the skin without innuction.

The aerated dry foam delivery system was proved quite satisfactory because of marked advantages like saving of time over conventional application of cream, sufficiently strong & flexible to be secured over the wound site, gives adequate cover to the wound thereby preventing environmental mycrobial invasion and by virtue of hydrophilic nature water loss could be maintained at a satisfactory level. This report describes the *in-vitro* and *in-vivo* comparative evaluation of medicated cream and dry film,

Materials & Methods

Formulation of dry foam :—The formula adopted by catania and king[2] was used with slight modification as the film was somewhat tough in nature. Therefore, 5% of glycerol was added to give flexibility to the preparation.

Dextran *, 4 gm, was dissolved in 19 ml of distilled water maintained ar 70—75°C. To this solution were added 2 ml of sorbitol solution, 1 ml of glycerol & 0.5 ml of soya lecithin solution. The whole solution was whipped for 10 minutes with electric stirrer and the resultant foam was spread into a petridish to a depth of about 3—4 mm and dried at 40—45°C until a smooth film was cast. Three batches of this this film containing 0.5, 1 and 2 % w/v of AgSD added prior to whipping, were prepared.

Infra-red moisture balance was used to find the moisture content & average value was found to be 8.5%. Care was taken to heat at low temperature to avoid caramelization of dextran. Disk of dry foam of 1 cm diameter when put in 1 ml of distilled water at ambient temperature dissolved in 15—18 seconds.

In-Vitro Evaluation

20 ml of melted nutrient agar was poured into sterile petridishes 100 × 15 mm. To which was added 0.1 ml of broth suspension of overnight inoculum of *Pseudomonas aeruginosa* containiug approximately 5×10^7 organisms/ml just before the congealing point of agar media approached. The media was allowed to set.

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* Dextran was extracted from Lomodex 10% in Dextrose with methanol. Lomodex-Rallis India Ltd, West Bengal.

Six holes of 6 mm diameter were formed in the agar with sterile cork borer. Then by means of tared 5 ml syringe, a calculated amount of the cream samples (0.5, 1 and 2% w/v) were added to each well and incubated overnight at 37 (±1)°C. Zones of inhibition were measured with Anti-biotic Zone Reader. For medicated dry foam, the same procedure was utilized except in place of well, disks of dry foam with 6 mm diameter were placed an agar aseptically. Non-medicated dry foam served as control. The results of above *in-vitro* study are given in Table I.

In-Vivo Evaluation

The burned, infected guinea pig was selected as the animal model. The dorsum of animal was depilated with Anne French to make it clear and smooth. Reproducible burns were inflicted on the dorsum with a steel rod of 6mm diameter dipped in a reservoir of distilled water maintained as 75 (±2)°C under ether anesthesia The rod was directed on back for ten second to obtain four fullthickness thermal injuries. The animals were then caged individually and given food and water allotments ad lib. Observations made after 24 hours revealed uniform burns with sharp margins.

Now the three burns on each animal were seeded by swabbing with a 18 hours culture of *Pseudomonas aeruginosa* with viable count approximately 5 x 10^7 organisms/ml; the fourth one served as uninfected control. Out of three infected burns, one was applied with 0.125gm of 1% Ag SD cream with sterilized spatula. The second was medicated with 1% AgSD dry foam with one cm diameter and third was held as burned infected infected control. Treatment ment with other samples were done in the above same fashion.

The effectiveness of formulations was studied by taking swab cultures from the burn every 24 hours immediately prior to medication. A standard sterilized cotton tipped applicator after wetting with sterilized saline was twirled on the open wound for 5 seconds to obsorb maximum number of organisms. This swab tip was then broken into a tube containing 25 ml of sterilized saline & then shaken thoroughly for half an hour. 0.1 ml of this suspension was then spread over the agar plate, which was incubated overnight to see the presence of bacterial colonies. The results of in-vivo study are given in table II.

Table I

In-Vitro Comparative Evaluation of Ag SD Cream & Dry Foam.

Formulation	n	Diameter of zone of inhibition (± S E M) in cm.	Student's 't' test
0.5% Ag SD Dry Foam	15	1.75 ± 0.0486	P>0.05
0.5% Ag SD Cream	15	1.53 ± 0.0319	
1.0% Ag SD Dry Foam	15	2.54 ± 0.0372	P<0.001
1.0% Ag SD Cream	15	1.74 ± 0.0624	
2.0% Ag SD Dry Foam	15	2.63 ± 0.0433	P<0.001
2.0% Ag SD Cream	15	2.16 ± 0.0392	
Dry Foam Control	5	--	
Cream Control	5	—	

S E M Standard error mean, n = No. of experiments performed.

Table II

In-Vivo Comparative Evaluation of Ag SD Dry Foam and Cream

Total animals	Individual animal	No. of days post-burn with negative Pseudomonas culture after treatment with		Student's 't' test
		Ag SD Dry Foam	Ag SD Cream	
8	1	3	7	P<0.001
	2	4	5	
	3	2	6	
	4	3	5	
	5	3	7	
	6	3	6	
	7	4	5	
	8	3	7	

Recognition of Pseudomonas

Recognition of Pseudomonas is dependent on the production of a blue-green foul smelling water soluble pigment known as pyocyanin. A more common one is a second pigment known as ppoverdin, a fluorescent pignment which fluoresces when examined under UV lamp. Therefore, the UV lamp exposure was done daily before the morning application of cream or foam.

Swab suspension of organism was also tested for Gram's staining and Oxydase test.

Results and Discussion

In-Vitro Comparative Evaluation of AgSC cream and Dry Foam

A comparative evluation of various samples of dry foam and cream revealed that the mean diameters of zone of inhibiton of dry foam are greater than those of corresponding cream. The dry foams have therefore an efficient release of AgSD, capable of securing the maximum antibacterial action from the quantity of agent present in the film.

The mean diameter of zone of inhibition measured 1.75 cm and 1.53 cm for 0.5% AgSD dry foam and cream respectively. Though the dry foam provided larger zones, the student's 't' test of the results did not show any significant difference ($p>0.05$). Therefore it can be assumed that dry foam is as effective as the cream.

The mean diameters of zone of inhibition for 1% and 2% AgSD dry foam measured 2.54 and 2.63 cm, which are quite larger than those of cream showing 1.74 and 2.16 cm. The student's 't' test showed a highly significant difference between the means of the data obtained ($P<0.001$) thus proving the dry foam to be a better formulation over the cream.

The *in-vitro* data clearly indicates that the drug release from dry foam is faster and better than cream. Thus the above therapeutic concept of medicated dry foam proved quite valid and effective.

In-Vivo Comparative Evaluation of AgSD Dry Foam & Cream

Pseudomonas burn wound sepsis is the primary concern for the considerable mortality. Since supera-eschar bacterial colonization is usually considered to be the first stage of sepsis, it was therefore assumed that the eradication of surface colonies would indicate the effectiveness of topical medication. Thus a swab culture form the local infection with no positive growth of Pseudomonas was selected as the basis for evaluation of dry foam and cream.

It is quite evident from the data that both the formulations, though at different time intervals, are effective on the burn with no positive culture. Student's 't' test reveals that dry foam inhibited the growth in shorter duration than the cream. One of the reason for this might be that the dry foam when applied relased the drug quickly with the dissolution of the film in the wound exudate.

To see the effect of spreading of AgSD from one place to another when the film dissolves in weeping wound, one of the burn was infected which acted as untreated control. The study revealed that there was no evidence of reduction in the count of Pseudomonas and the severity of infection was progressing. Therefore, it can be assumed that there was no diffusion of drug from one burn to another.

In burn injury, the cross contamination of causative organism is highly prevalent. To see the contamination from infected burn area to the adjacent area with no bacterial growth, the fourth burn on each animal was kept uninfected. It was observed that in the initial three days of theraphy there was no such migration of infection bus subsequently invasion from infected area to unseeded island was there. From this observation it is clear that such contamination occurs in burn injury trauma. This was further confirmed when the eyes of guinea-pigs also got infected lateron.

U. V. lamp examination of dorsum was done daily to see the presence of Pseudomonas. Areas which have not been treated with formulation showed marked fluorescence, while wounds applied with medicated cream or dry foam did not show any fluorescence, At the end of the experiment when the medication was stopped, all the four areas showed fluorescence indicating the presence of organism though they were finally medicated and cured.

After ten dayt of medication, the eschar became quite soft, pliable and could be easily removed. The underlying tissues looked exceptionally healthy and wound smear rarely showed any growth. As the eschar was cleared away, regeuerated island of epithelium became conspicuous.

Thus both the *in-vitro* and *in-vtvo* results suggest that medicated dry foam is a better formulation over the cream and may be tried on burned patient.

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