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EXPLORATORY DEVELOPMENT OF AN ULTRAFAST-CURING WOUND DRESSING

ANNUAL/FINAL REPORT

KURT DASSE
DONALD DEMPSEY
RAMACHANDRAN THIRUCOTE

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FOREWORD

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INTRODUCTION

This report summarizes research conducted on the contract DAMD17-88-8012 supported by USAMRDC, over the past three years directed towards developing antimicrobial dermal dressings (ADDs'). The dressings consist of a trilaminate composed of an outer medical grade polyurethane fabric, an acrylic-based pressure sensitive adhesive, and an antimicrobial impregnated polyurethane laminate which serves as a controlled drug release layer. The objectives in developing this new technology have been to create a medicated dressing that is:

- (1) easily applied under adverse climatic conditions,
- (2) highly compliant and abrasion resistant and
- (3) allows controlled release of antimicrobial agents over a seventy two hour period against a variety of microbial organisms.

The new dressing is capable of incorporating heat labile antimicrobial agents and releasing them in a controlled fashion when in contact with the wound. This was made possible by the development of a room temperature, rapid ultraviolet (UV) curable liquid polyurethane oligomer. The liquid mixture of urethane and drugs is cured under UV lights and the resultant monolithic film provides controlled release of the agents when placed on the wound. This targeted drug delivery minimizes many of the inherent problems associated with conventional systemic drug delivery.

The three year research program had been directed towards development of dressings which would be effective against a wide range of microorganisms. Several types of dressings were developed and tested; of these, two types of dressings were chosen for conducting preliminary shelf stability testing:

- (1) a dressing containing 30% chlorhexidine gluconate; and
- (2) a dual loaded dressing containing 20% silver sulfadiazine and 10% chlorhexidine gluconate.

Successful completion of all the proposed tasks during the course of the three years, has involved making the base oligomer, developing fabrication methods, developing methods to measure the antimicrobial agents, monitoring elution kinetics, optimizing drug release and supplying USAIDR with sterile dressings for in vivo evaluation of the technology.

The work resulted in the development of new techniques for drug analyses, improved fabrication methods for sustained release and better management of wound healing. Work in the latter portion of the contract was devoted to preliminary shelf stability testing. The final formulations were subjected to accelerated conditions for six months. The following report provides a detailed description of the studies carried out in the performance of this program.

BACKGROUND

The study of the environmental conditions under which the process of wound healing takes place is relatively recent. The process of wound repair and healing was known to consist of a chronological sequence of events (1). There was also an awareness that an open wound was subject to the threat of infection. Early studies showed that optimal wound healing occurred under a scab. As a result, dressings were used to protect the wound site from bacterial invasion and infection.

Research in the late sixties and early seventies showed that the optimum conditions for wound healing occurred under a dressing that maintained a moist environment (2). The development of the polyurethane products (a temporary artificial skin) for wound dressings arose from the attempts to provide a moist environment much like nature's blister (3).

Prior to the studies on the potential effects of dressings on the wound repair process, the medical community had thought that the surgical dressing mainly absorbed exudate, cushioned the wound site, and hid the site from the patient. This research illustrated that dressings can affect the response to the wound and even retard healing through dehydration or tissue damage during removal. Dressings can optimize epithelialization, reduce pain (which is associated with wound dehydration), and minimize local

inflammation. The dressings impregnated with drugs can also deliver medication (4).

Optimal wound healing occurs when the dressing material strikes a balance between dehydration and maceration (which results from accumulation of excess exudate). In addition to stimulating pain, dehydration leads to desiccation and cell death, undermining epithelial movement and wound closure. Prevention of dehydration can minimize eschar formation and inflammatory response. Maceration, which is stimulated by excess fluids and debris, is often accompanied by bacterial proliferation which retards the wound healing process (5).

Currently available wound dressings are primarily limited to gauze pressure bandages. These materials have minimal beneficial characteristics. The dressing materials function as simple coverings that are not impervious to microorganisms, thereby providing little protection from infection. By being absorbent, these dressings may desiccate the wound thus delaying healing. The material absorbed into the dressing may provide an ideal substrate for supporting microbial growth. These materials may also provide a mild degree of hemostasis via the application of pressure. However, pressure must be maintained for long periods.

The desired balance between dehydration and maceration has had a direct impact on the development of synthetic dressings. The

moist healing environment (to counter dehydration) has been the primary goal of materials development. Permeability to vapor (to counter maceration) has been an influential factor in the development of most of the materials.

One of the most successful commercial dressing for split-skin graft donor sites and burn care is Op-Site^R (Smith & Nephew). Op-Site is a polyether-based, moisture-vapor permeable polyurethane membrane compounded with silica gel. The polyurethane membrane is hydrophilic, and is coated at the edges with a polyvinyl ethyl ether adhesive (6). Op-site has been shown to offer significant advantages over conventional dressings in the management of superficial injuries, split-skin graft donor sites, and burn sites (6):

- A) the hydrophilic polyurethane dressing protects wounds from bacterial contamination, while providing a suitable environment for rapid wound healing;
- B) patients seem more comfortable with the polyurethane dressing than with standard bandages; and
- C) rapid healing is produced by enhancement of re-epithelialization through increased mitotic division and migration of epidermal cells.

However, Op-Site has several disadvantages:

- 1) it is not amenable for self application;
- 2) it adheres tenaciously to both intact skin and the scab. During

removal, not only is the patient subjected to acute localized pain, but the wound site frequently starts rebleeding when the scab is forcibly disturbed; and

3) it is non-medicated.

The new wound dressing developed at TCI is a self-adherent, medicated dressing capable of being applied to the wound by the injured individual. This wound dressing is fabricated from a UV curable polyurethane and can incorporate antibiotics or antimicrobials. The release of drugs from the dressings is controlled to last at least 72 hours. Figure 1 illustrates a cross section of the TCI Antimicrobial Dermal Dressing (ADD), showing the liner reflected back, exposing the antimicrobial loaded controlled release layer. The backing material is made of a flexible, nylon reinforced semi-permeable polyurethane membrane.

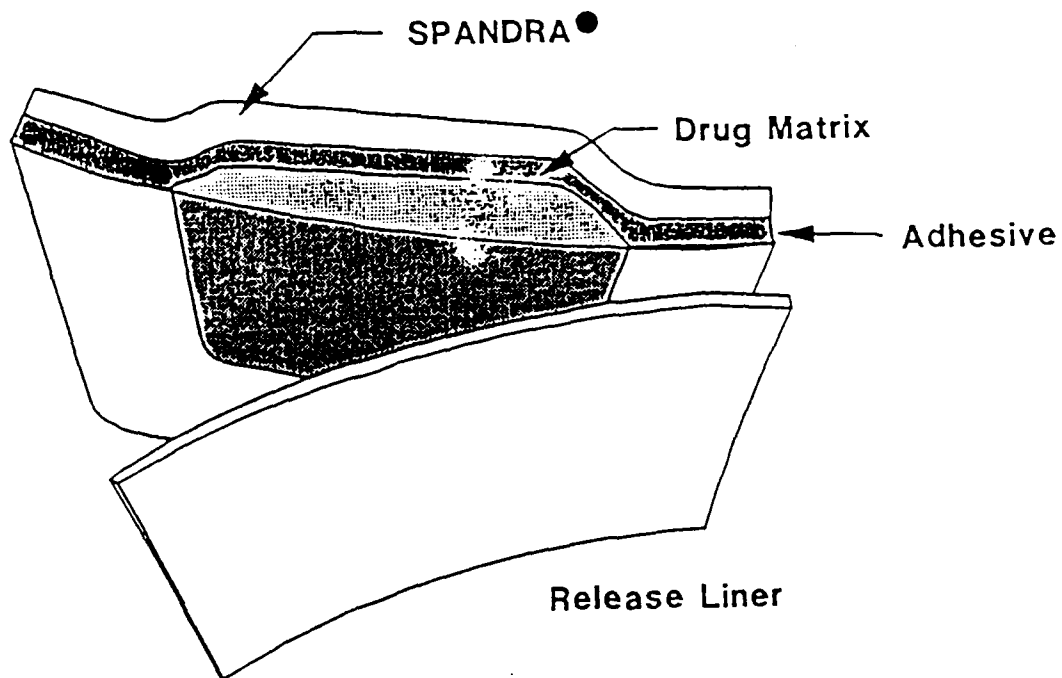


Figure 1. Cross Sectional Illustration of the TCI Antimicrobial Dermal Dressing with the Antimicrobial Controlled Release Layer Exposed.

SUMMARY OF WORK PERFORMED

The research was performed as tasks over the three years of the contract. The several tasks performed during each year are briefly described here.

A major task for Year 1 was the synthesis and manufacture of the UV curable polyurethane oligomer. The vinyl terminated urethane oligomer was synthesized from three reactants: isophorone diisocyanate, polypropylene glycol and hydroxyethyl methacrylate. The photoinitiator was added to this finished product to produce the UV curable property. Once the formulation was identified, ample quantities of the oligomer were produced at the beginning of each contract year to complete the work load.

The wound dressings tested in vivo, on guinea pigs at USAIDR laboratories exhibited a tendency to adhere to the wound. Removal often resulted in the dislodging of blood clots and bleeding. However, the use of a silicone gum or fluid in the dressing helped to prevent this adhesion. The silicone fluid when incorporated into the oligomer migrated to the surface and formed a nonadhesive film which facilitated easy removal of the dressing. The purpose of task 2 was to identify the loading of silicone fluid in the oligomer required to prevent adhesion to the wound. Various levels of low viscosity medical grade silicone fluid (Dow Corning DCO 200) ranging from 2% to 5% by weight were incorporated into the

oligomer. The results of the ensuing tests demonstrated that the 2% load of silicone fluid was sufficient to provide the adequate degree of release (7).

The dressing is attached to the skin by means of an adhesive. The selection of this adhesive was based upon several factors namely:

- (1) adhesivity to skin
- (2) cohesive strength
- (3) shear strength
- (4) irritancy and
- (5) shelf stability.

Thirty dressings incorporating varying quantities of silicone were tested for adhesive characteristics by USAIDR and these results were reported (7).

Wound dressings should allow the permeation of gases but at the same time provide a moisture barrier. The backing material used to fabricate the wound dressing was tested for its permeation characteristics and these results were reported (7).

The next phase in the development of the wound dressing was the incorporation of suitable antimicrobial agents. Two antibiotics, gentamicin sulfate and clindamycin phosphate were the initial drugs of choice. These two antibiotics were incorporated into the oligomer and fabricated into dressings. These dressings

were tested for release kinetics in vitro using Franz diffusion cells. Methodology was developed for the analysis of each antibiotic. The maximal loading was established, and the dressings incorporating this load were tested by USAIDR in vivo to establish efficacy parameters under task 5.

Eleven tasks were successfully completed during the second year. Task 1 of Year 2 focused on optimizing the release of the antibiotics from the dressing as well as adhesion to the skin. Several innovative techniques were utilized to optimize the efficiency of the wound dressing namely:

- (1) improve dispersion of the drugs in the matrix
- (2) increasing the potency of the antibiotics
- (3) increasing contact surface area
- (4) increasing hydrophilicity and
- (5) increasing the thickness of the dressing.

These techniques were evaluated in vitro and the optimized dressings were tested at USAIDR (8).

The adhesive tested in Year 1, though very aggressive on dry skin, was not effective on moist or wet surfaces. The adhesive had to adhere to moist skin, since the wound dressing was required to be used under all climatic conditions. Several types of adhesives were tested for their wet and dry strength and a suitable candidate was chosen (8). This adhesive was used for all subsequent formulations tested by USAIDR.

Dressings incorporating several different formulas were fabricated and tested at TCI. The in vitro tests resulted in the development of new and/or modified analytical techniques for the analysis of the antibiotics (8). Five formulations incorporating gentamicin sulfate and clindamycin phosphate were fabricated for testing in vivo at the USAIDR facility in Maryland. These dressings were also extracted for residual drug content after application on wounded guinea pigs.

The antibiotics used in the wound dressings are very potent. However, these agents are specific in their bacteriocidal action and have no activity against fungi. The in vivo tests conducted on guinea pigs demonstrated the specific spectrum of activity of each antibiotic. The specificity limited the use of these drugs as universal candidates for dressings. Hence the shelf stability of the dressings incorporating these antibiotics was not assessed.

Other suitable agents had to be chosen for incorporation into the dressing matrix. A candidate of choice was chlorhexidine gluconate, a wide spectrum antimicrobial solution with bacteriocidal and fungicidal properties. Lyophilization techniques assisted the incorporation of this drug into the polymer matrix. The effective use of formulating principles optimized the release of chlorhexidine gluconate from the dressing (9). In vitro microbiological plate assays helped demonstrate the efficacy of these dressings. Five formulations incorporating lyophilized

chlorhexidine gluconate were tested on guinea pigs by USAIDR. The optimal formulation was selected for testing shelf life.

Microbiological plate tests are a useful tool in establishing the effectiveness of an antimicrobial agent against specific strains of microorganisms. These techniques were employed to select an agent, or a combination of agents, for incorporation into the wound dressing to combat a broader microbial spectrum (9).

Based on the microbiological plate tests, a dually loaded dressing incorporating silver sulfadiazine and chlorhexidine gluconate was selected, as well as a triple loaded combination incorporating these two agents along with clindamycin phosphate. The agents were successfully incorporated into the polymer and prepared for subsequent testing.

The successful development of several prototype formulations resulted in the initiation of the last phase of the contract. Two prototype formulations were selected and the exploratory shelf stability studies performed. The shelf stability was performed under accelerated conditions so that a reasonable prediction of shelf life could be obtained.

EXPLORATORY SHELF STABILITY STUDIES

Degradative chemical reactions in formulations take place at definitive rates. They depend on such conditions as concentration of reactants, temperature, pH, radiation, etc. An effective and efficient study of these reactions by the application of physicochemical principles has made it possible to predict the stability of a drug product at normal shelf storage conditions from drug products stored under exaggerated conditions.

The evaluation of temperature dependency of a formulated product is useful to determine the rate of degradation. This permits the prediction of stability for the product at ordinary shelf temperatures from accelerated conditions. The most commonly used method for expressing the influence of temperature on chemical reaction is the relationship proposed by Arrhenius (10).

The utility of the temperature dependency relationship depends on the controlling mechanism of the degradation process. In solutions, there is a considerable change in the heat of reactions at elevated temperatures. This makes the mathematical prediction very reliable. On the other hand, where the heat of activation is very small, the effect of temperature is negligible and use of the Arrhenius predictions can be erroneous.

Graphic methods, based on the Arrhenius principles are more

simplistic and can be used under a wide range of conditions. Several graphic techniques have been employed to predict the breakdown that may occur over prolonged periods of storage at normal shelf conditions (11). One of the popular methods plots the fractional life period or the time required for the drug to decompose to a fraction of the original potency, versus the reciprocal of the absolute (K) temperatures. The time for the degradation or reduction in concentration at several temperatures to reach a predetermined theoretical potency is noted. These log time values at several temperatures are plotted and the time for the concentration to reach this point at room temperature can be obtained from the resulting straight line by extrapolation.

The performance of the tasks during the three years of the contract resulted in the development of two prototype formulations. The final phase of the program was initiated after the prototype formulations were selected. This phase required the manufacture and fabrication of large quantities of ADDs'. The batch sizes for tasks VI and X had to be 3 to 4 times larger than the batch sizes for tasks IV and VIII. Five hundred ADDs' each, of 30% loaded chlorhexidine gluconate as well as the dual combination containing 20% silver sulfadiazine and 10% chlorhexidine gluconate were fabricated, hermetically packaged and sterilized by radiation techniques. An exploratory stability study was performed on these prototype ADDs'. A group of forty-eight randomly sampled ADD's from each of the two prototype formulations were placed under each of

the five conditions specified below:

- (1) 45° C, 90% R.H,
- (2) 38° C, 90% R.H,
- (3) Room Temperature
- (4) 23° C, under water,
- (5) -40° C.

The dressings from each of these two batches (Batch Nos. 008081-PDDS1 - 30% chlorhexidine gluconate and 010181-PDDS2 - 20% Silver sulfadiazine and 10% chlorhexidine gluconate) were tested for in vivo efficacy by USAIDR at the beginning of the six month period to establish baseline parameters. The in vitro testing was performed every two months for six months for each of the ADDs' and the results of these tests are reported here. At the end of the six month period, the dressings exposed to the several conditions were delivered to USAIDR for in vivo evaluation.

1. Chlorhexidine gluconate ADDs'

The chlorhexidine gluconate ADDs' incorporated 30% lyophilized chlorhexidine gluconate powder in the polymer matrix. The stability of these chlorhexidine gluconate ADD's was determined using two methods:

1. analyzing the drug for the presence of p-chloroaniline (PCA) a degradation product, and
2. measuring the maximum amount of chlorhexidine gluconate

eluted from the ADD's over 72 hours.

The second method for determining storage stability involves an analysis of elution data acquired from ADD's removed from each of the storage conditions. The elution kinetics were recorded documenting the initial time point ($t = 0$) for the samples undergoing accelerated shelf stability. The elution kinetics of the samples subjected to the accelerated conditions at the 2, 4 and 6 month intervals were then compared to the samples at time $t = 0$.

2. Dual Loaded ADDs'

The dual loaded ADDs' incorporated 20% micronized silver sulfadiazine and 10% lyophilized chlorhexidine gluconate in the polymer matrix. The stability of these ADDs' was determined for each of the two antimicrobial agents separately. The stability profile of the lyophilized chlorhexidine gluconate was determined by the methods used for the single loaded ADD incorporating chlorhexidine gluconate. The silver sulfadiazine concentration in the ADDs' was determined by the drug elution rate profiles (9). This HPLC assay is the only method available for the determination of silver sulfadiazine, though it does not determine the concentration of free silver caused by drug degradation. However, silver sulfadiazine has been shown to be stable for at least two years in the solid state (12).

Results

1. Chlorhexidine gluconate ADDs'

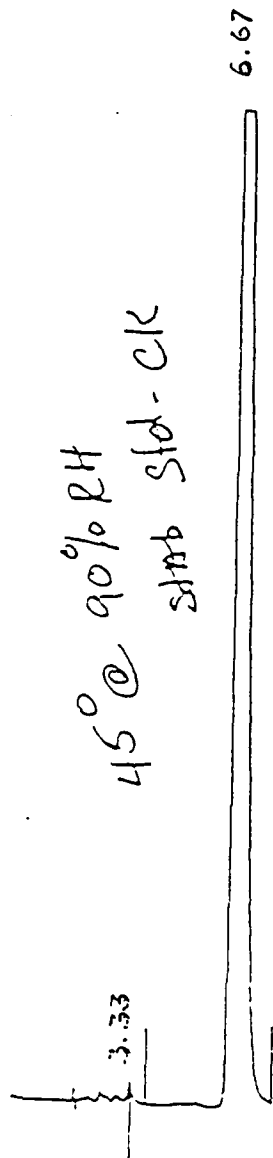
The chlorhexidine gluconate ADD's were subjected to quality control tests. The accelerated stability tests conducted showed that chlorhexidine gluconate is stable even when stored at 45° C for six months. Results of the assay showed p-chloroaniline to be under 10 mcg/ml; Figure 2 represents a chromatogram depicting this result. Figure 3 represents a chromatogram of a 1000 mcg/ml chlorhexidine gluconate standard spiked with p-chloroaniline. A comparison of these two chromatograms confirmed that chlorhexidine gluconate stored at 45° C for six months exhibits very little degradation products; the maximum PCA recorded was less than 10 mcg/ml.

The chlorhexidine dressings exhibited efficacy in the microbiological zone of inhibition testing and complied to the sterility tests at the end of the six (6) month storage period; these results along with the certificate of analysis, are appended (Appendix II).

The baseline release profile ($t = 0$) of the chlorhexidine ADD's is shown in Figure 4. Figures 5, 6 and 7 illustrate data obtained for the ADD samples subjected to the accelerated conditions (-40° C, 23° C under water, ambient, 38° C and 45° C) at

2, 4 and 6 month intervals respectively. The tabulated results for the dressings are summarized in Appendix III.

INJECT



FEB. 23, 1991	15:43:47	CHART 0.50CM/MIN	CALC #0
		RUN #93	OPR ID 6
COLUMN		SOLVENT	
EXTERNAL STANDARD QUANTITATION			
PEAK #	AMOUNT	RT	EXP RT
	32.32900	3.33	AREA
	11358.64900	6.67	32529 L
			11358649 L
TOTAL	11711.00000		RF
			0.0000000E0
			0.0000000E0

Figure 2. Chromatogram of Lyophilized Chlorhexidine Gluconate Stored at 45°C for Six Months

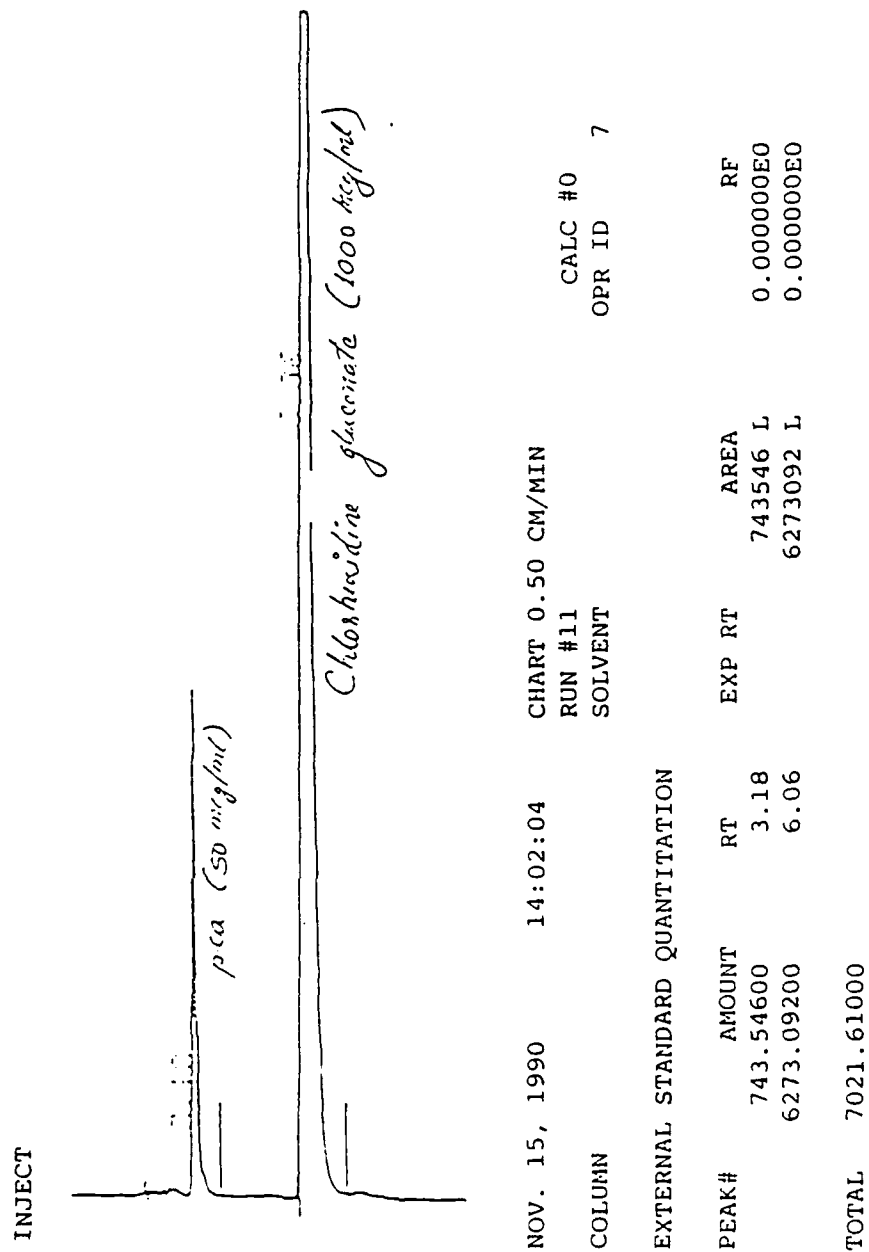


Figure 3. Chromatogram of Chlorhexidine Gluconate Standard (1000 mcg/ml) Spiked with p-chloroaniline (50 mcg/ml).

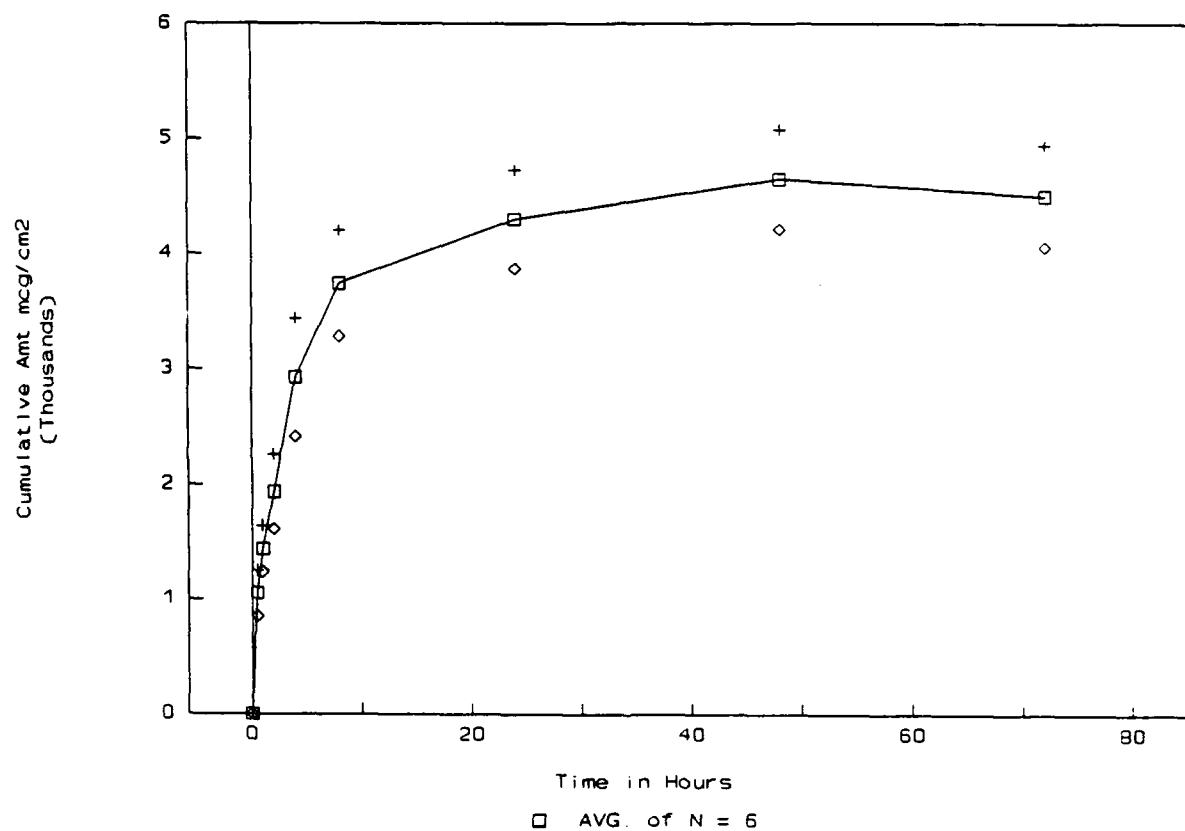


Figure 4. Release Profile of 30% Chlorhexidine Gluconate ADD's After E-beam Sterilization. Stability Samples at Time $t = 0$.

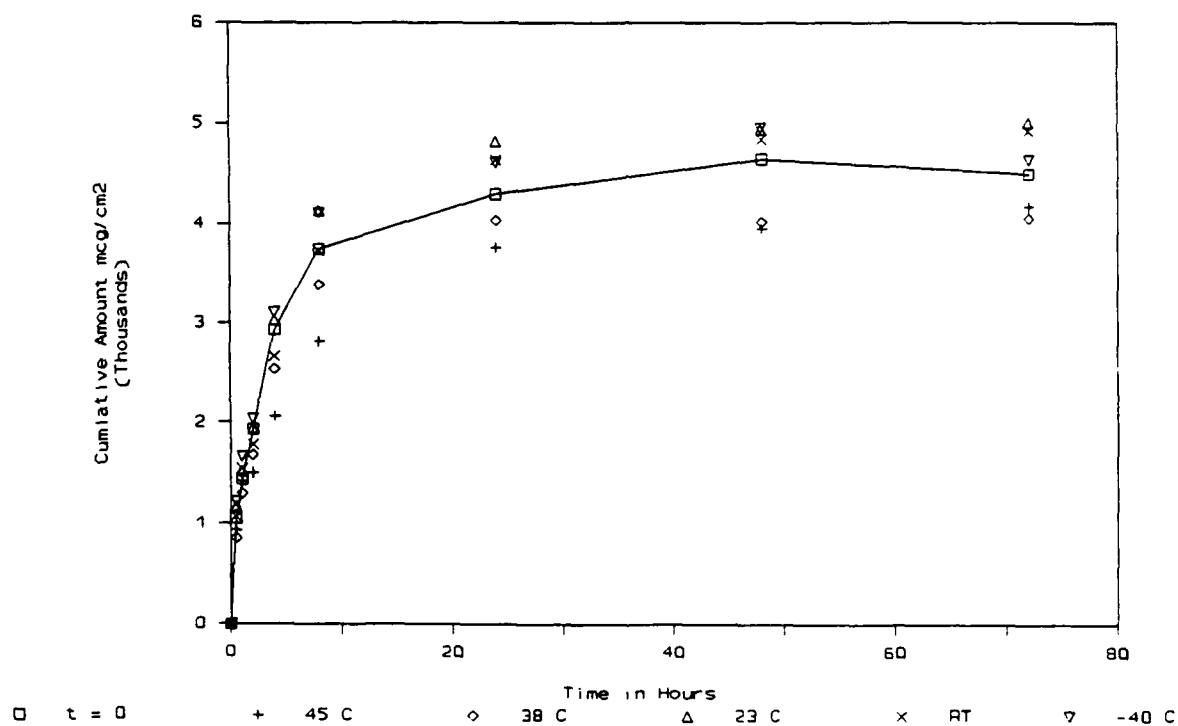


Figure 5. Release Profile of 30% Chlorhexidine Gluconate ADDs' Subjected to Accelerated Storage Conditions at 2 months.

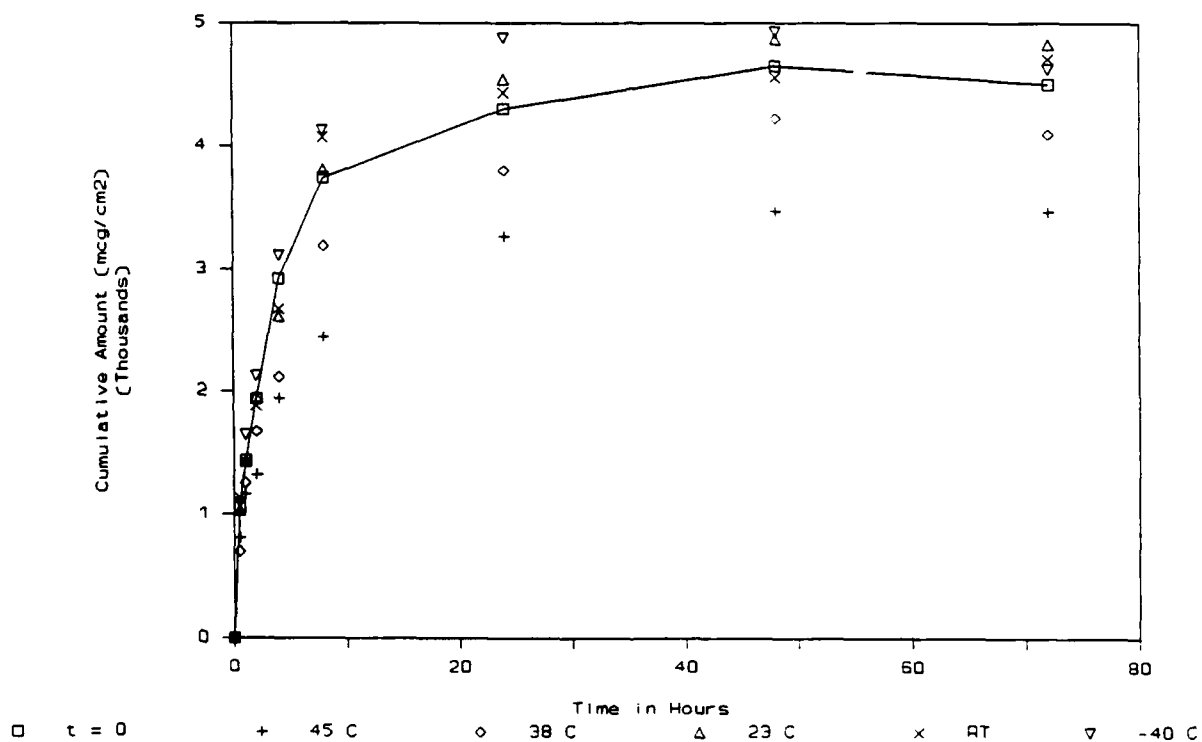


Figure 6. Release Profile of 30% Chlorhexidine Gluconate ADDs' Subjected to Accelerated Storage Conditions at 4 months.

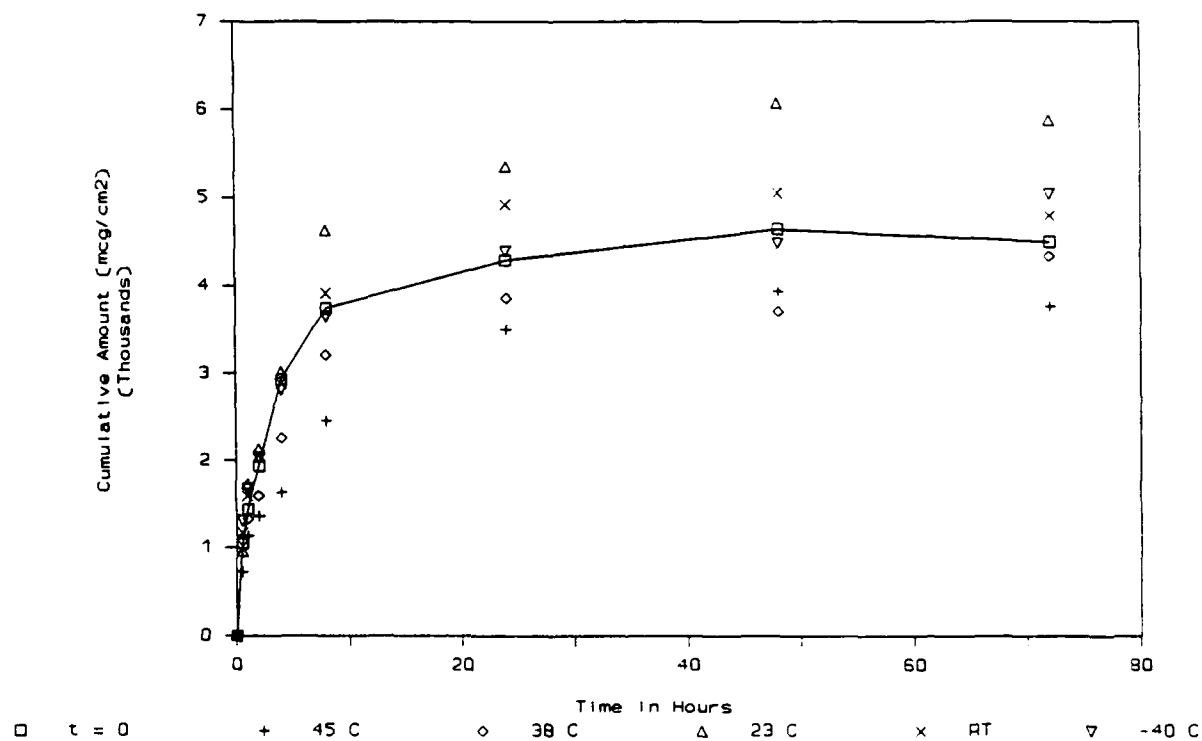


Figure 7. Release Profile of 30% Chlorhexidine Gluconate ADDs' Subjected to Accelerated Storage Conditions at 6 months.

2. Dual Loaded ADDs'

The dual loaded ADDs' were subjected to various tests in the laboratory (9). The ADDs' subjected to higher temperatures were noticeably dark in color on visual inspection. The elution rates for the silver sulfadiazine portion was also higher. However, the chromatographic analysis of the eluates demonstrated no detectable degradation of the chlorhexidine gluconate content. Figures 8 and 9 illustrates the baseline release profiles for the dual loaded ADD's at time $t = 0$, for chlorhexidine gluconate and silver sulfadiazine respectively.

Figures 10, 12 and 14 illustrate the elution profiles of chlorhexidine gluconate from the ADDs' at 2, 4 and 6 month intervals. Figures 11, 13 and 15 illustrate the elution rate profiles for the silver sulfadiazine from the dual loaded ADDs' at 2, 4 and 6 month periods. The tabulated results are included in the Appendix.

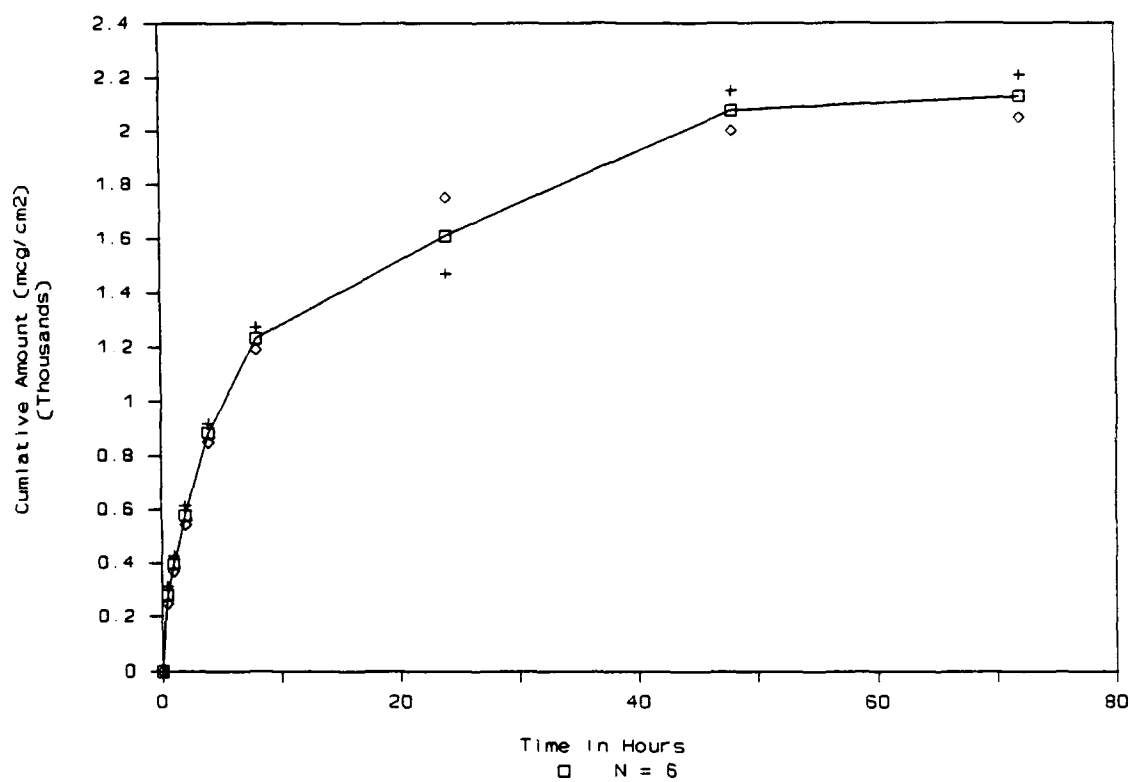


Figure 8. Release Profile of Chlorhexidine Gluconate from the Dual Loaded ADDs' at $t = 0$.

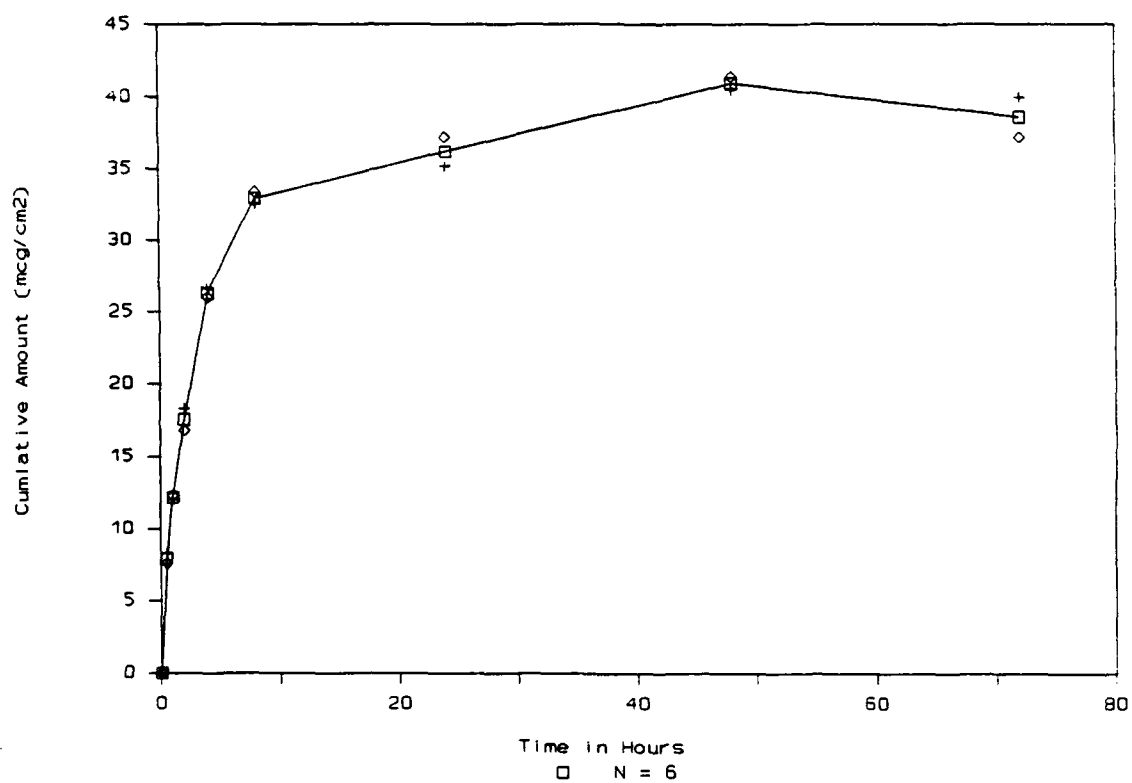


Figure 9. Release Profile of Silver Sulfadiazine from the Dual Loaded ADDs' at $t = 0$.

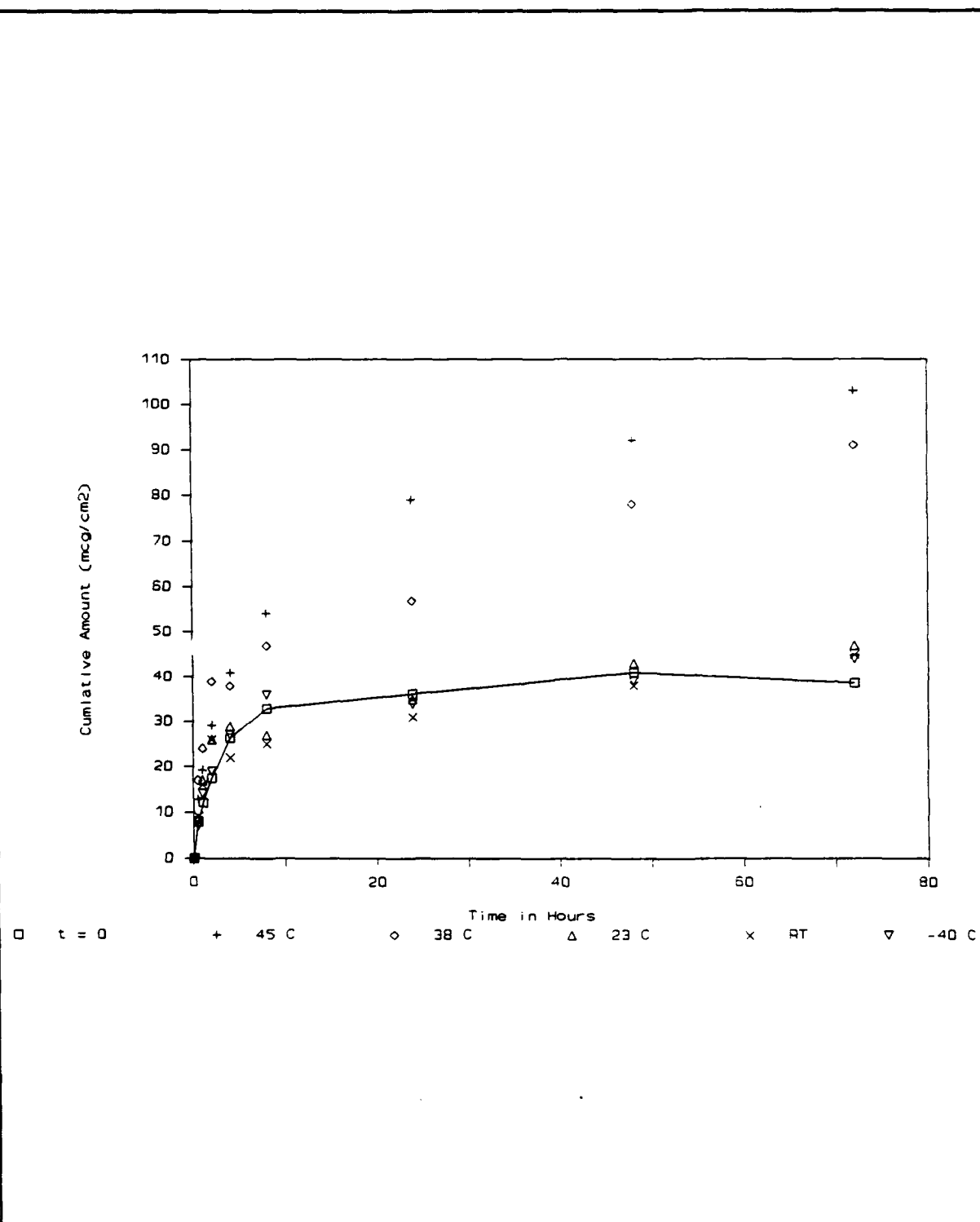


Figure 11. Release Profile of Silver Sulfadiazine from the Dual Loaded ADDs' at t = 2 months.

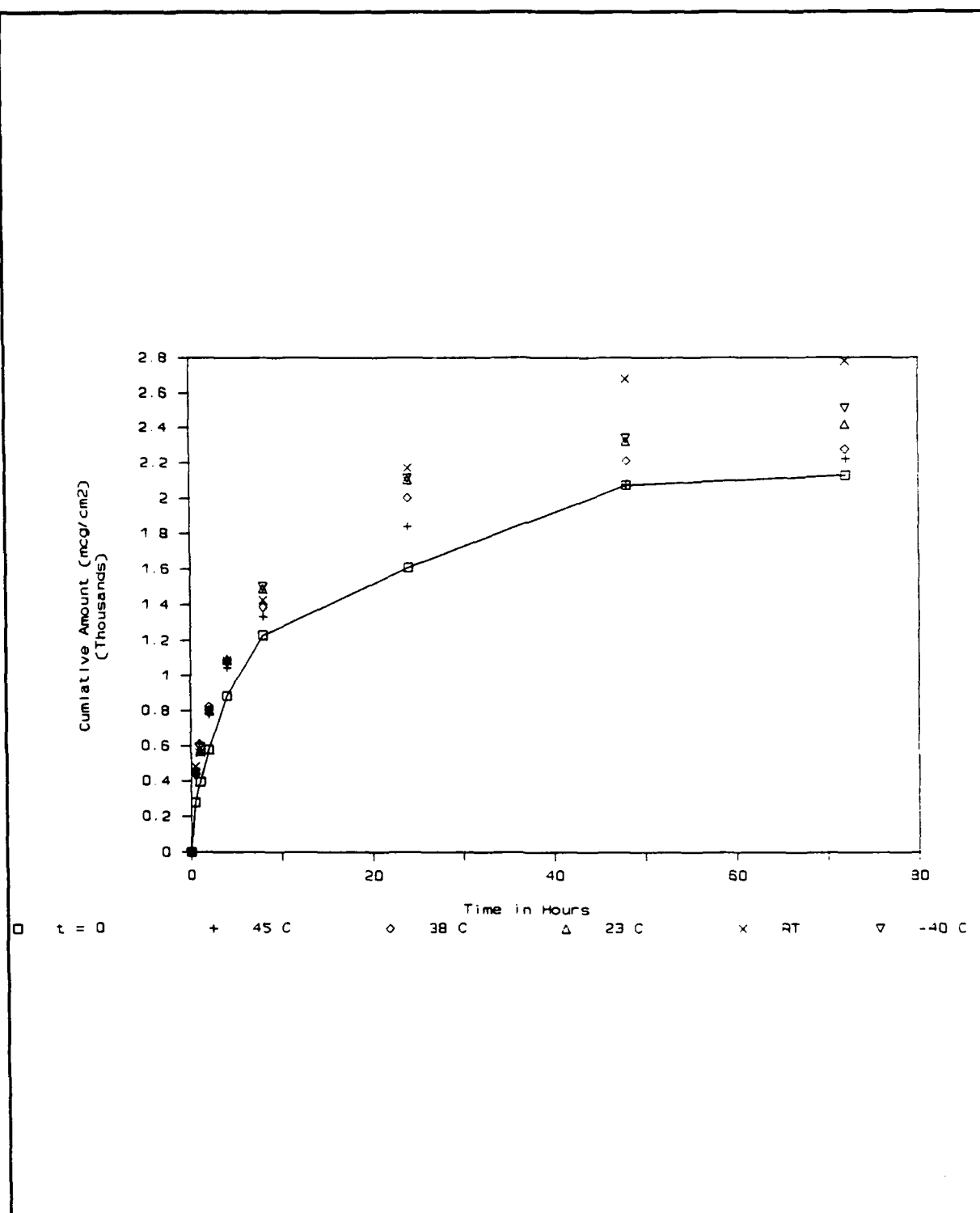


Figure 12. Release Profile of Chlorhexidine Gluconate from the Dual Loaded ADDs' at $t = 4$ months.

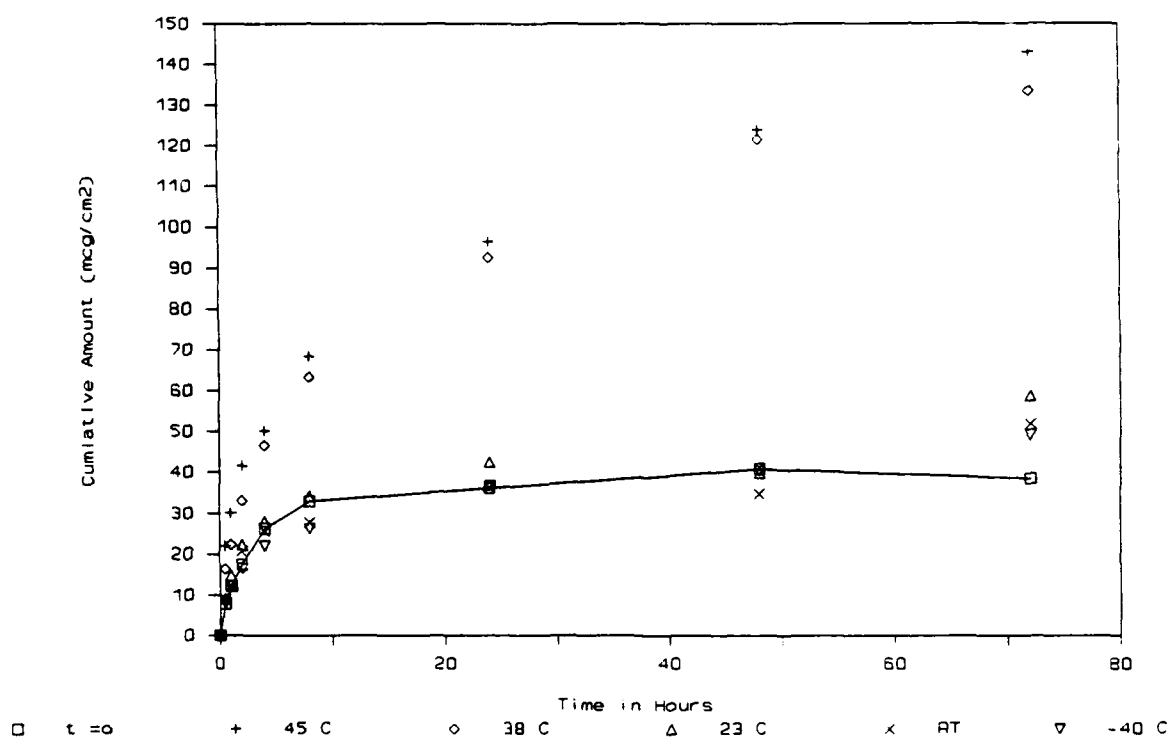


Figure 13. Release Profile of Silver Sulfadiazine from the Dual Loaded ADDs' at t = 4 months.

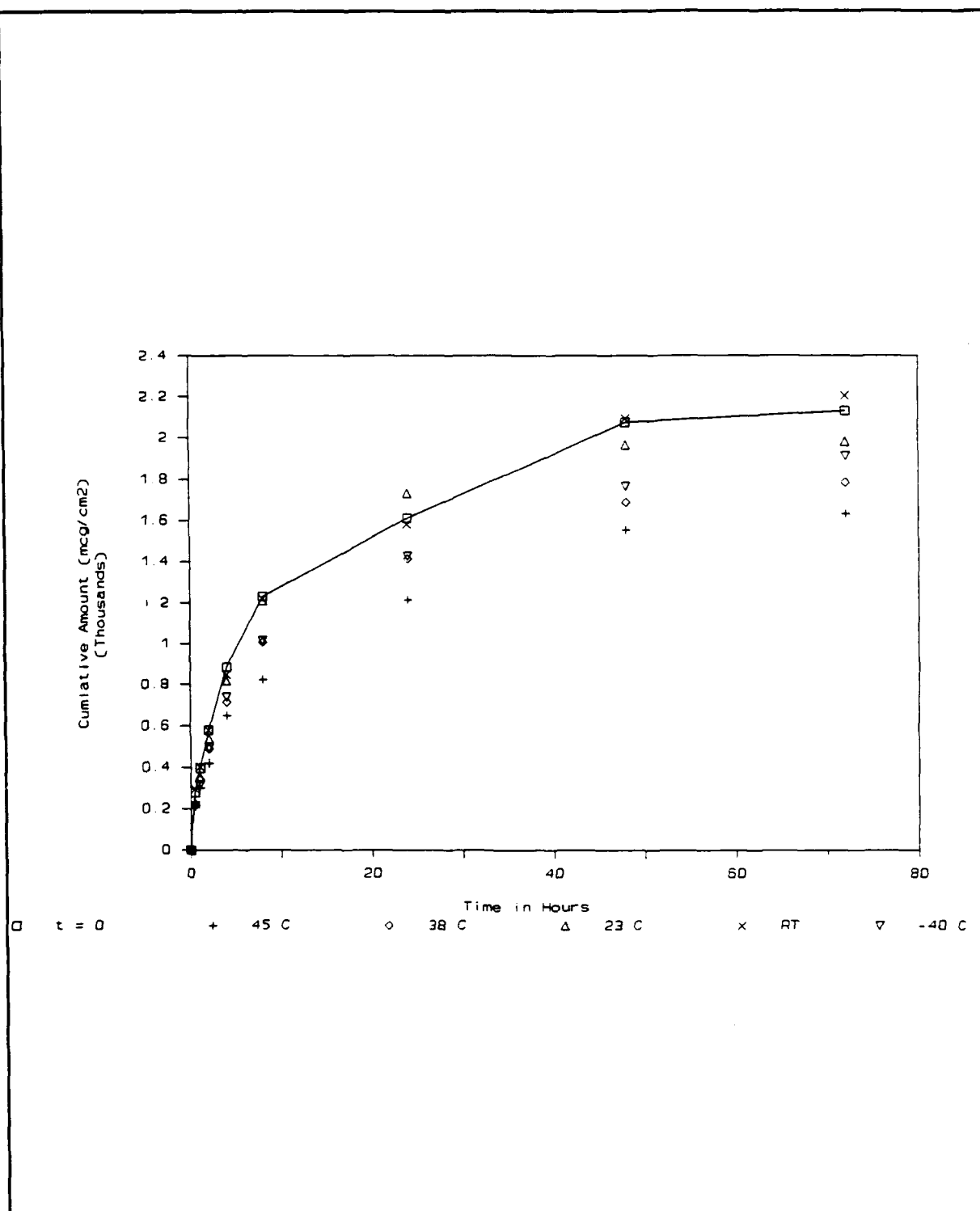


Figure 14. Release Profile of Chlorhexidine Gluconate from the Dual Loaded ADDs' at t = 6 months.

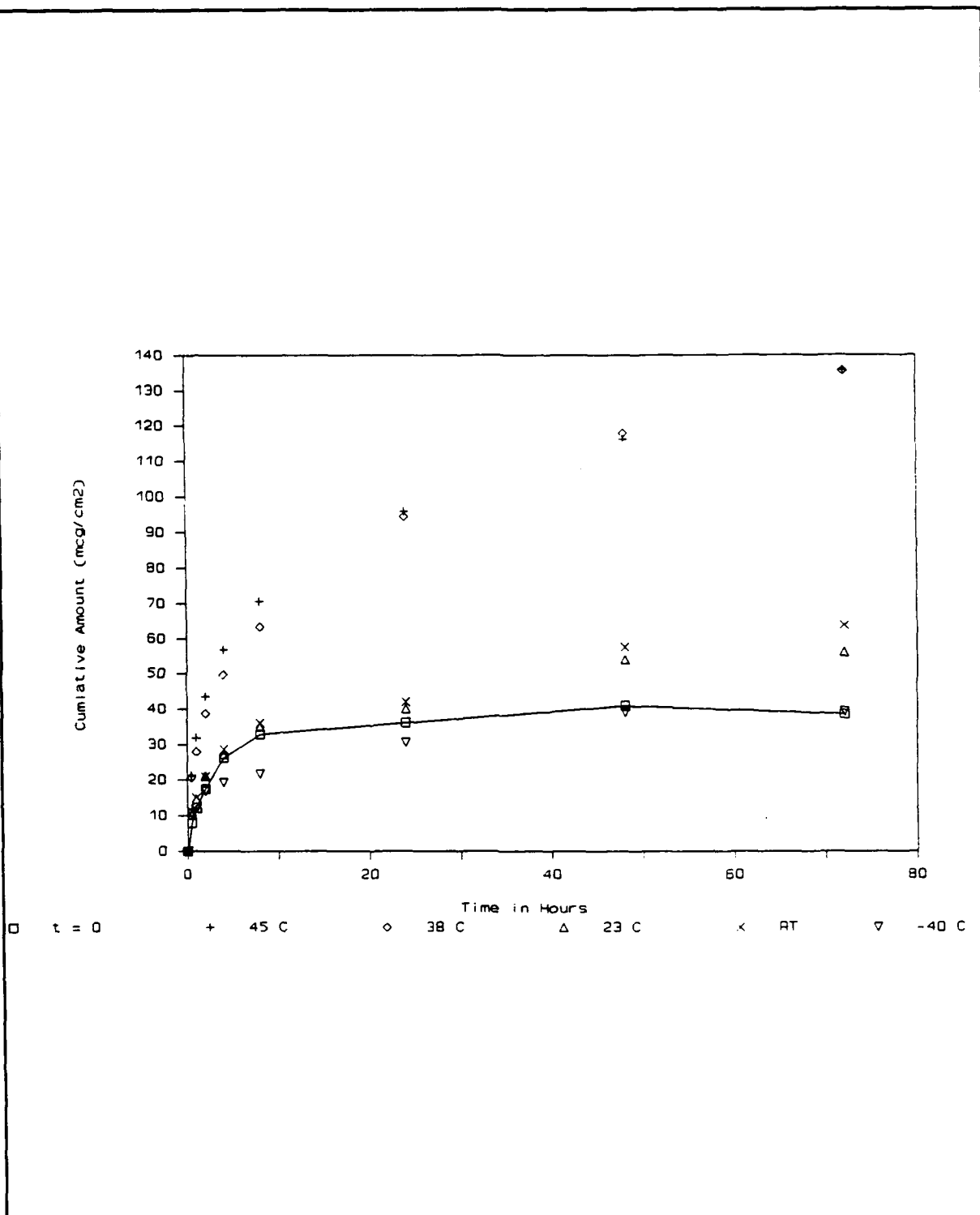


Figure 15. Release Profile of Silver Sulfadiazine from the Dual Loaded ADDs' at t = 6 months.

Discussion

The chemical stability of chlorhexidine gluconate was tested using chromatographic techniques. Chlorhexidine gluconate was found to be 99.5% stable even when stored at high temperatures. Since the degradation reaction was negligible, the release of the drug from the polymer matrix over a period of time became the determining factor.

The graphical method was adopted for predicting the shelf stability of chlorhexidine gluconate ADDs'. It was hypothesized that to demonstrate in vivo efficacy, the in vitro release profile of the ADD should show at least 3000 mcg/sq. cm. after 72 hours. This was considered to be the minimum effective concentration (MEC) of the drug to be released in vitro, for the ADDs' to be effective in vivo. This was determined from the in vivo trials conducted earlier (9). The 6 mil thick dressing (Formulation 2) demonstrated effectiveness when tested on guinea pigs. This dressing released approximately 3000 micrograms/sq. cm. in 72 hours or about 64% of the 12 mil dressing tested for shelf stability (Figure 16). This in vitro release profile of the 6 mil thick ADD (or 64% of 12 mil samples at $t = 0$) was used as the MEC of the drug to be released from the dressing.

The elution profiles of the ADDs' subjected to the varying storage temperatures at periodic intervals were then plotted

(Figures 4, 5, 6 & 7). Figure 17 compares the elution rates of the ADD's at $t = 0$, to those stored at 45°C and -40°C for 2, 4 and 6 months. The ADD's stored at -40°C show no change in the elution rates over the control ($t = 0$). The ADD's stored at elevated temperatures (45°C), show a decrease in the elution rates. The logarithmic percent of the cumulative amount of the drug released from the ADDs' compared with those of the ADDs' at time $t = 0$, was plotted against time in days (Figures 18, 19, 20 and 21). The time for the concentration to fall to 3000 micrograms per square centimeter of the original concentration was then read from the graphs generated using trend analysis of Harvard Graphics software program. The log time to 3000 mcg/cm² was then plotted against $1/T$, and the extrapolation from 25°C (3.36×10^3) to the time (Y axis) predicts the shelf life of the product in days (Figure 22). The shelf life of the ADDs' stored under normal conditions was estimated to be about 800 days or over two years.

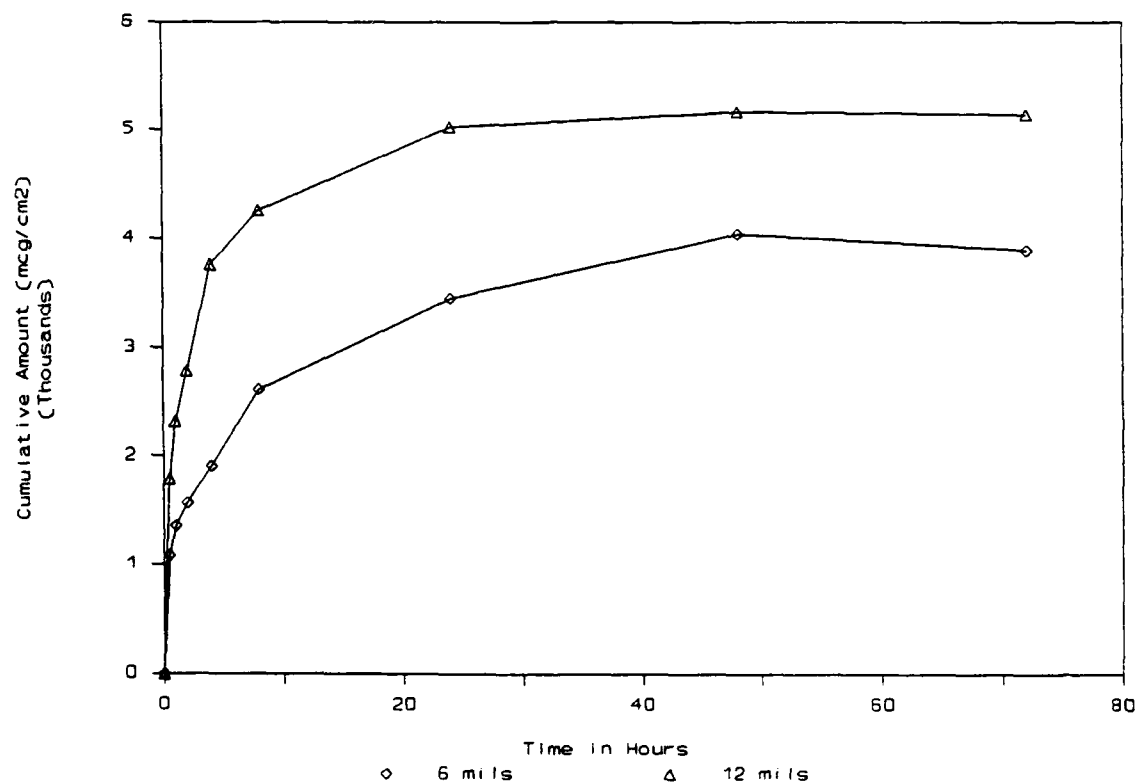


Figure 16. Drug Elution Profile of 30% Chlorhexidine Gluconate ADDs'- 6 and 12 mils thick: Formulation 2 and 5.

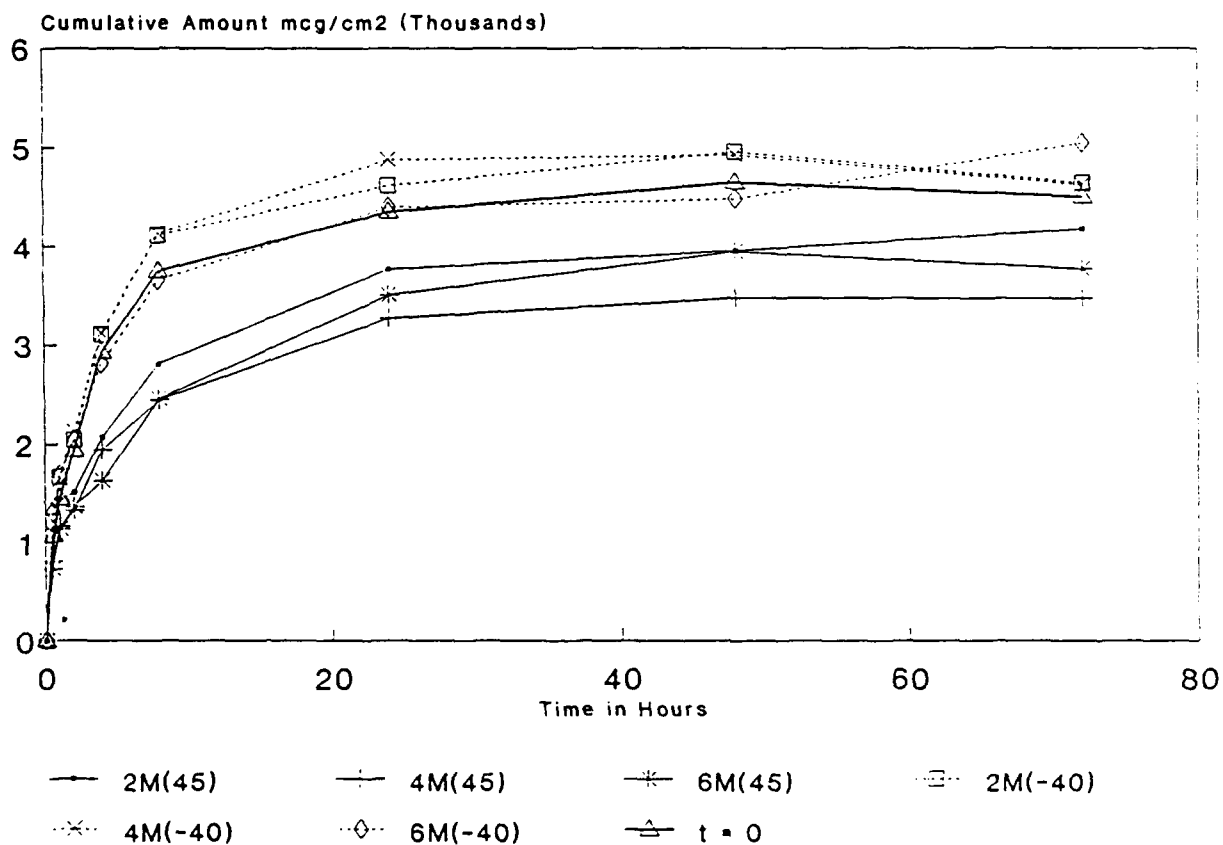
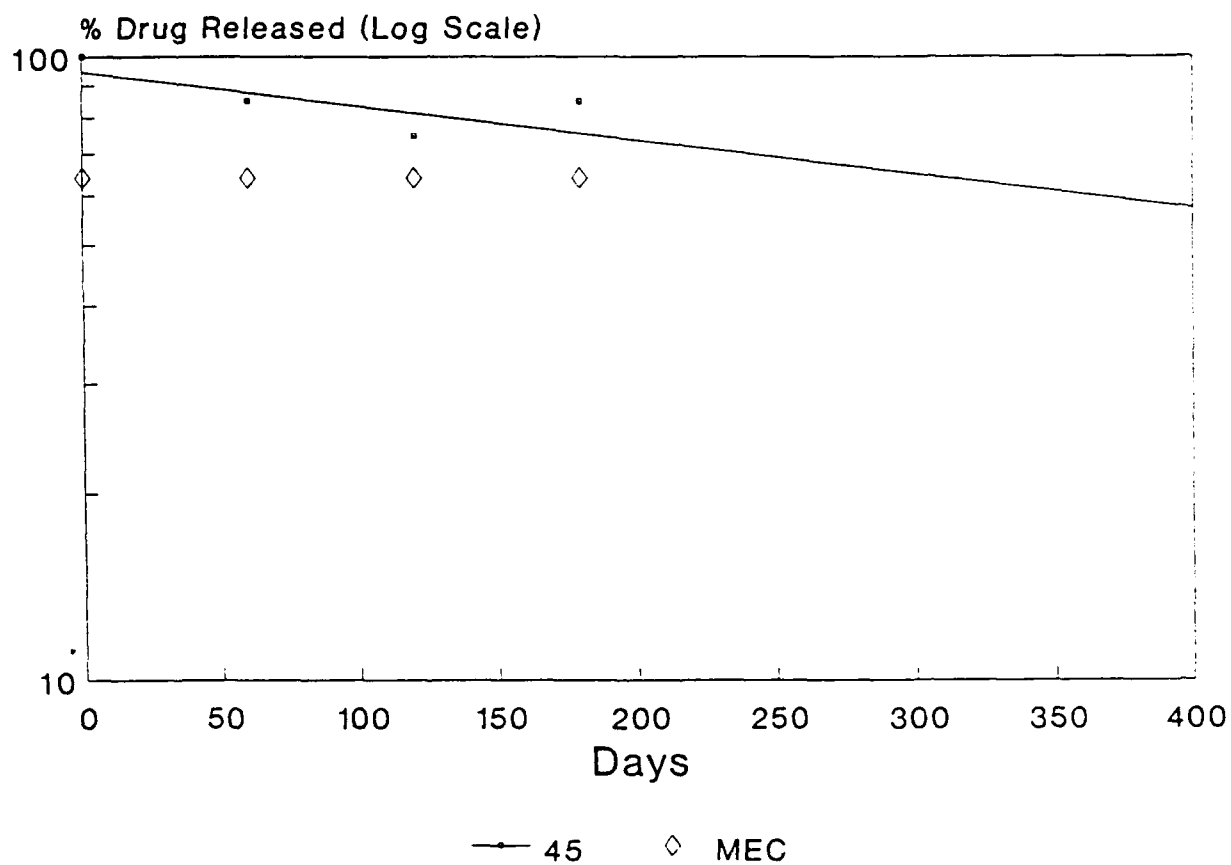
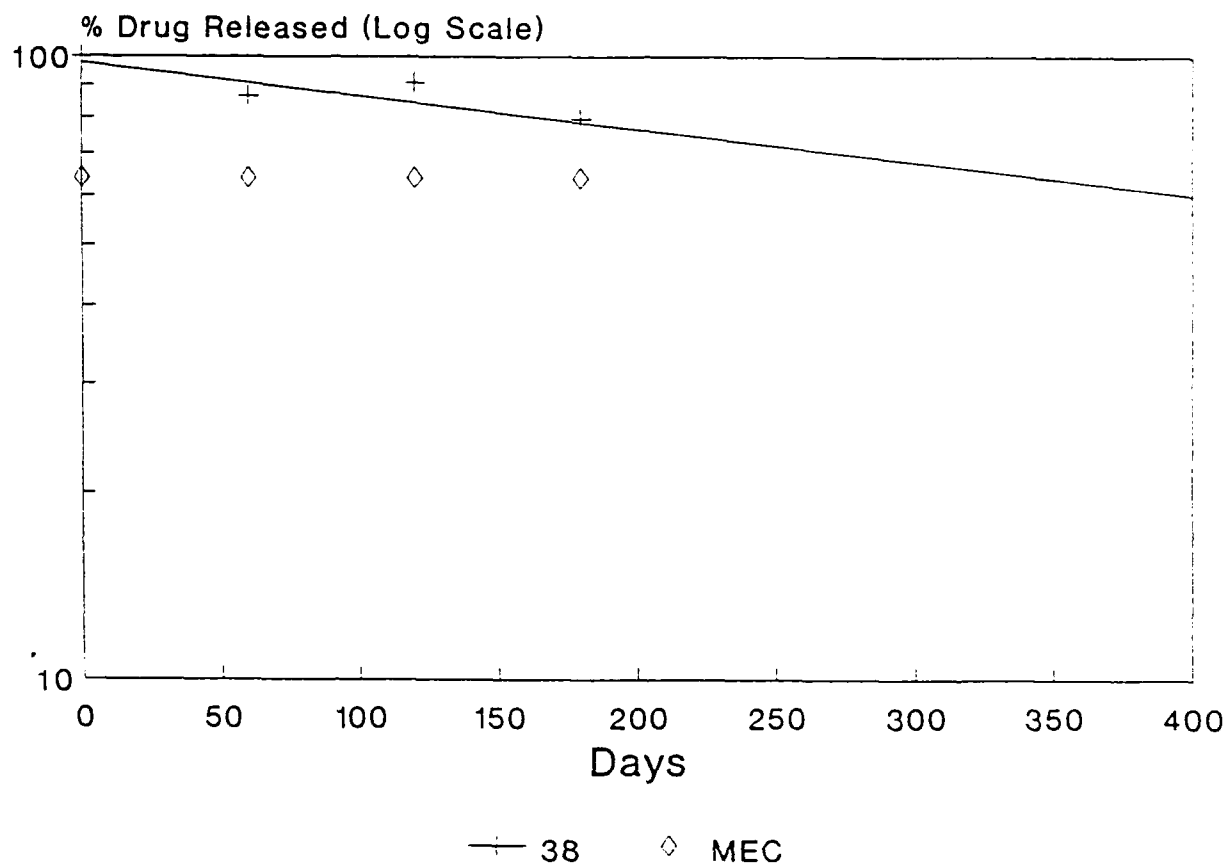


Figure 17. Elution Rates for the 30% Chlorhexidine Gluconate ADD's at $t = 0$ and Stored at the Temperature Extremes (-40°C and 45°C) for 2, 4 and 6 Months.



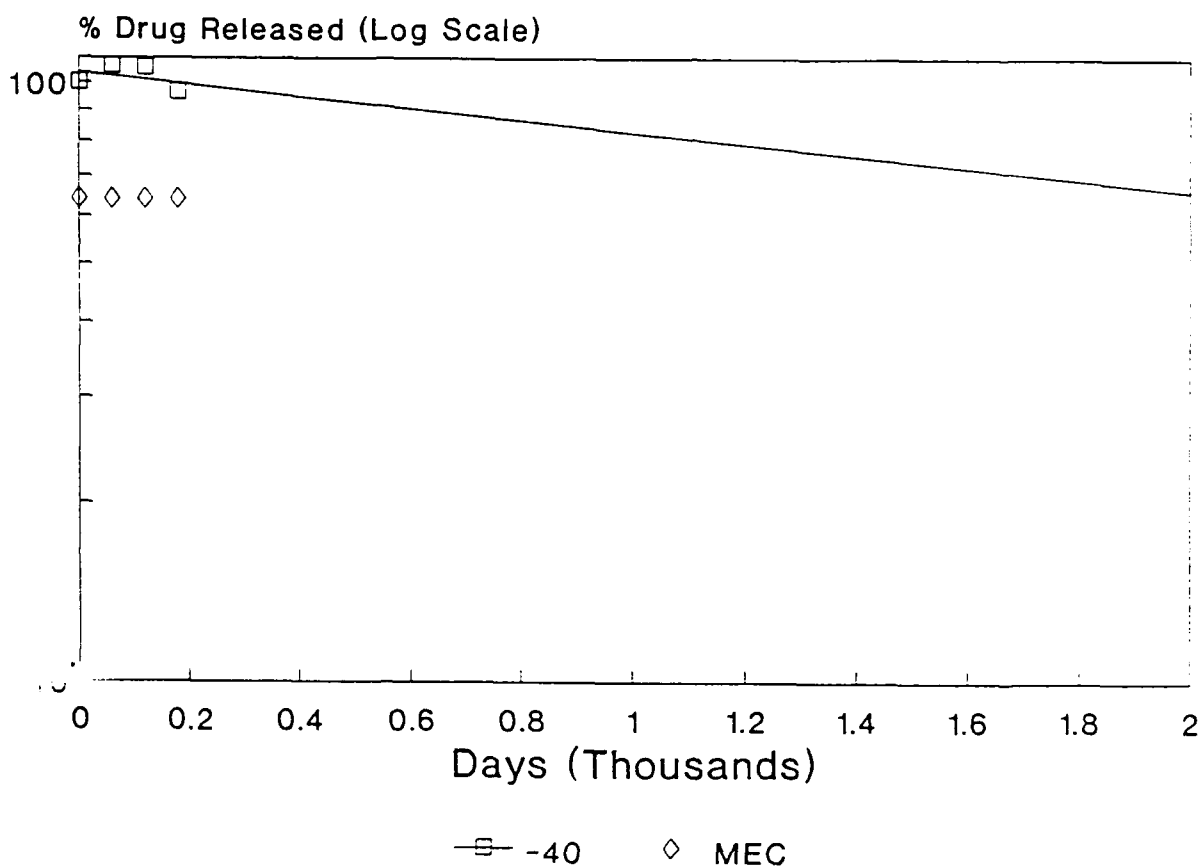
30/CHX

Figure 18. Shelf Stability Prediction for Chlorhexidine Gluconate ADDs'; Plot of Log Percent Drug Released Versus Time in Days for Samples Stored at 45°C.



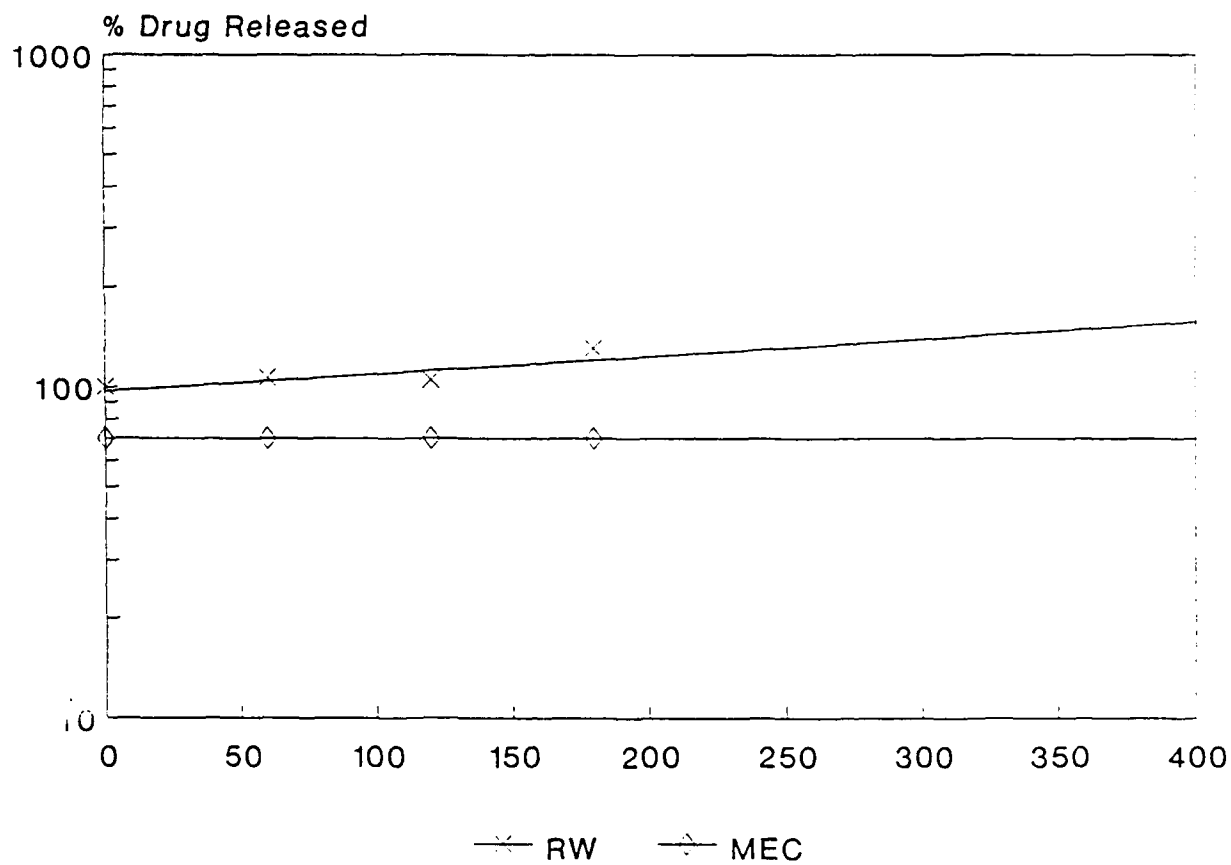
30/CHX

Figure 19. Shelf Stability Prediction for Chlorhexidine Gluconate ADDs'; Plot of Log Percent Drug Released Versus Time in Days for Samples Stored at 38°C.



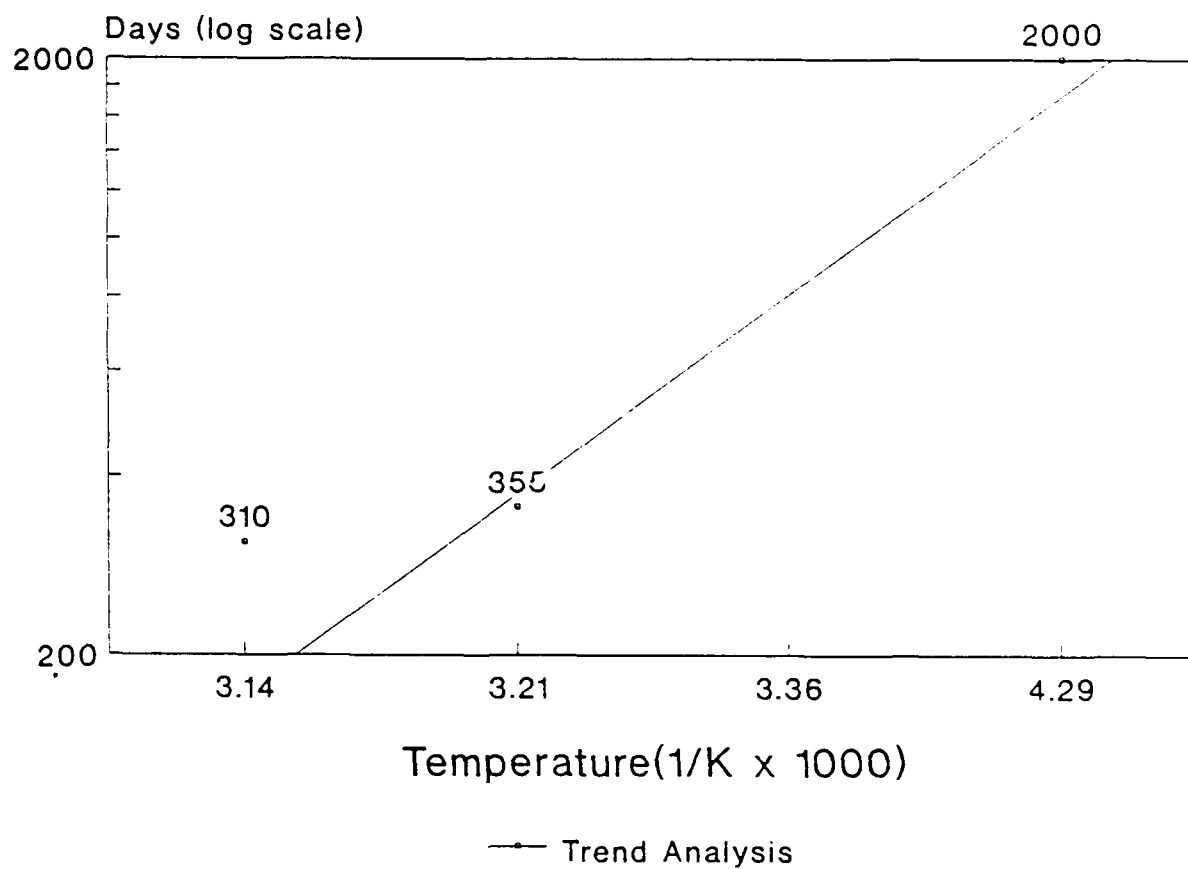
30/CHX

Figure 20. Shelf Stability Prediction for Chlorhexidine Gluconate ADDs'; Plot of Log Percent Drug Released Versus Time in Days for Samples Stored at -40°C.



30/CHX

Figure 21. Shelf Stability Prediction for Chlorhexidine Gluconate ADDs'; Plot of Log Percent Drug Released Versus Time in Days for Samples Stored at 23°C Under Water.



30/CHX

Figure 22. Shelf Stability Prediction for Chlorhexidine Gluconate ADDs' Stored Under Normal Shelf Conditions.

The analysis of the elution samples for the 30% loaded chlorhexidine gluconate ADD's did not show any detectable amount of PCA. The same HPLC methodology was used to predict the shelf life of chlorhexidine gluconate in the dual loaded ADDs'. The dual loaded ADDs' incorporated only 10% of the lyophilized powder and HPLC analysis indicated these were also free of degradation products.

The physical examination of dual loaded ADDs' subjected to high temperatures showed a discoloration of the dressing. The chromatographic analysis of the eluates did not show any degradation products for chlorhexidine gluconate. Mixtures of the drug powders were subjected to the same temperature conditions and analyzed by HPLC. This analysis showed the concentrations of both drugs remained constant which indicates the absence of any interactive product.

The silver sulfadiazine elution curves for every condition showed an overall increase from the original value at $t = 0$. The increase in the concentration of silver sulfadiazine in the elution samples for the dual loaded ADDs' is attributable to its solubility in the L62 excipient. Elevated temperature increases the rate at which the drug reaches the saturation concentration. This is demonstrated by the increase in the elution rate of silver sulfadiazine stored at 38 and 45°C (Figures 11, 13 and 15).

The ADD's subjected to the elevated temperatures turned dark brown in the island portion of the dressing. The in vitro microbiological zone of inhibition tests showed the efficacy of the dressings stored at elevated conditions. Also, literature states that the microbiological activity and efficacy of silver sulfadiazine is not compromised by strong color formation. Silver sulfadiazine in the solid state turns slightly yellow within one day upon exposure to light and remains in that state for at least two years. The extent of color formation increases with rise in temperature, but with no changes in silver and sulfadiazine content (12).

The graphical method used for predicting shelf life of chlorhexidine gluconate ADD's is dependant on the decrease in elution rates over time. This method is applicable for the elution rate of chlorhexidine gluconate in the dual loaded ADD's. However, the elution rate of silver sulfadiazine increases over time at elevated temperatures and the graphical prediction would show an infinite shelf life.

A dual loaded ADD incorporating 10% chlorhexidine gluconate should demonstrate an acceptable shelf life, since the 30% chlorhexidine gluconate ADD demonstrated a two year shelf life without any indication of degradation. This is verified by the elution data previously given where no appreciable decrease in the amount of drug eluted can be ascertained. The elution rate of

silver sulfadiazine from the dual ADD's increases with time, therefore, by definition these will have a satisfactory shelf life. The absence of any discernable interaction between the two drugs as determined by HPLC, also supports this. Finally, the in vitro zone of inhibition tests indicate these ADD's maintain efficacy after 6 months storage.

CONCLUSIONS

TCI has developed two prototype sustained release Antimicrobial Dermal Dressings. Both types of dressings incorporate antimicrobial agents to prevent infection up to 72 hours.

The first formulation, a 30% loaded chlorhexidine gluconate ADD, was formulated and tested successfully on guinea pigs. This dressing was effective in vivo against Strep. pyogenes, Staph. aureus and P. aeruginosa under prophylactic conditions. An exploratory accelerated stability study has demonstrated an effective two year shelf life for this product.

The second formulation, a dual loaded ADD incorporating 20% silver sulfadiazine and 10% chlorhexidine gluconate was also formulated and tested on guinea pigs. This dressing was effective against Staph. aureus and P. aeruginosa when used prophylactically. However, the effectiveness of this dressing against Candida is yet to be evaluated in vivo. These dressings were also subjected to exploratory shelf stability studies and demonstrated a two year shelf life for the product.

In conclusion, all tasks have been successfully completed. The prototype dressings have been shown to meet the design requirements of being easy to apply and effective against selected organisms.

RECOMMENDATIONS

The application for an Investigational New Drug (IND) for either of these two prototype dressings requires the statistical validation of the processes involved. This statistical validation was beyond the scope of this contract. All further work should address process validation.

The processing of the ADD's was dependent upon the quality of the lyophilized chlorhexidine gluconate powder (LCHX). There were occasions where the LCHX agglomerated during the dispersion stage of the process. Once the powder had agglomerated it could not be reworked even using elevated temperatures. Strategies to eliminate this problem should be defined.

Reaction rates double for every 10 degree increase in temperature. Both formulations of dressings have shown that storage at -40°C does not compromise their efficacy. It is recommended that future storage stability tests include an additional elevated temperature in order to give three data points above room temperature. This will facilitate predictions of shelf life under accelerated conditions.

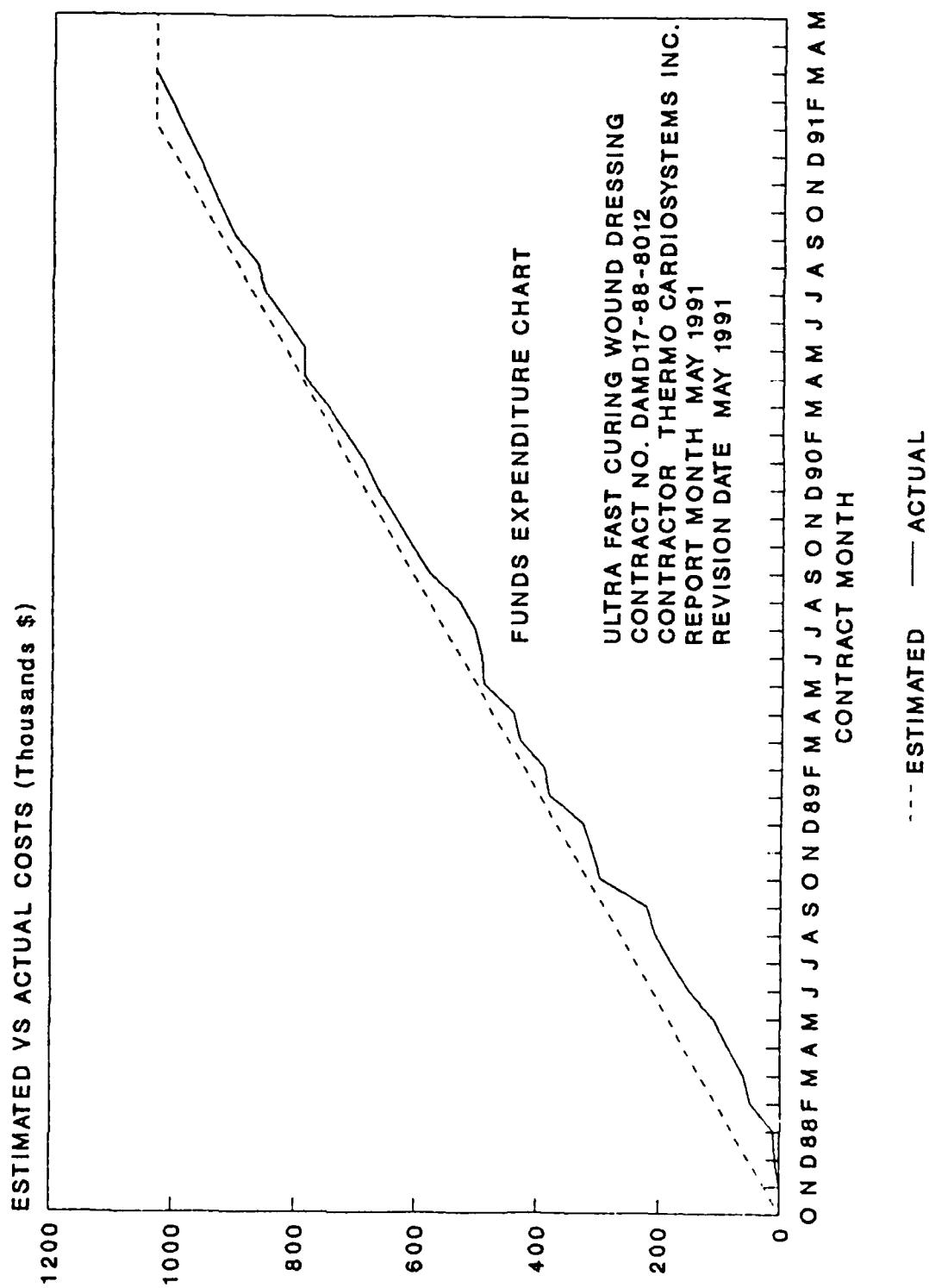
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8. K. Dasse, D. Dempsey and R. Thirucote, USAIDR Contract No. DAMD17-88-C-8012, Exploratory Development of an Ultra-Fast-Curing Wound Dressing, Annual Report, November 30, (1989), pp 1 - 87.
9. K. Dasse, D. Dempsey and R. Thirucote, USAIDR Contract No. DAMD17-88-C-8012, Exploratory Development of an Ultra-Fast-Curing Wound Dressing, Annual Report, November 30, (1990), pp 1 - 99.
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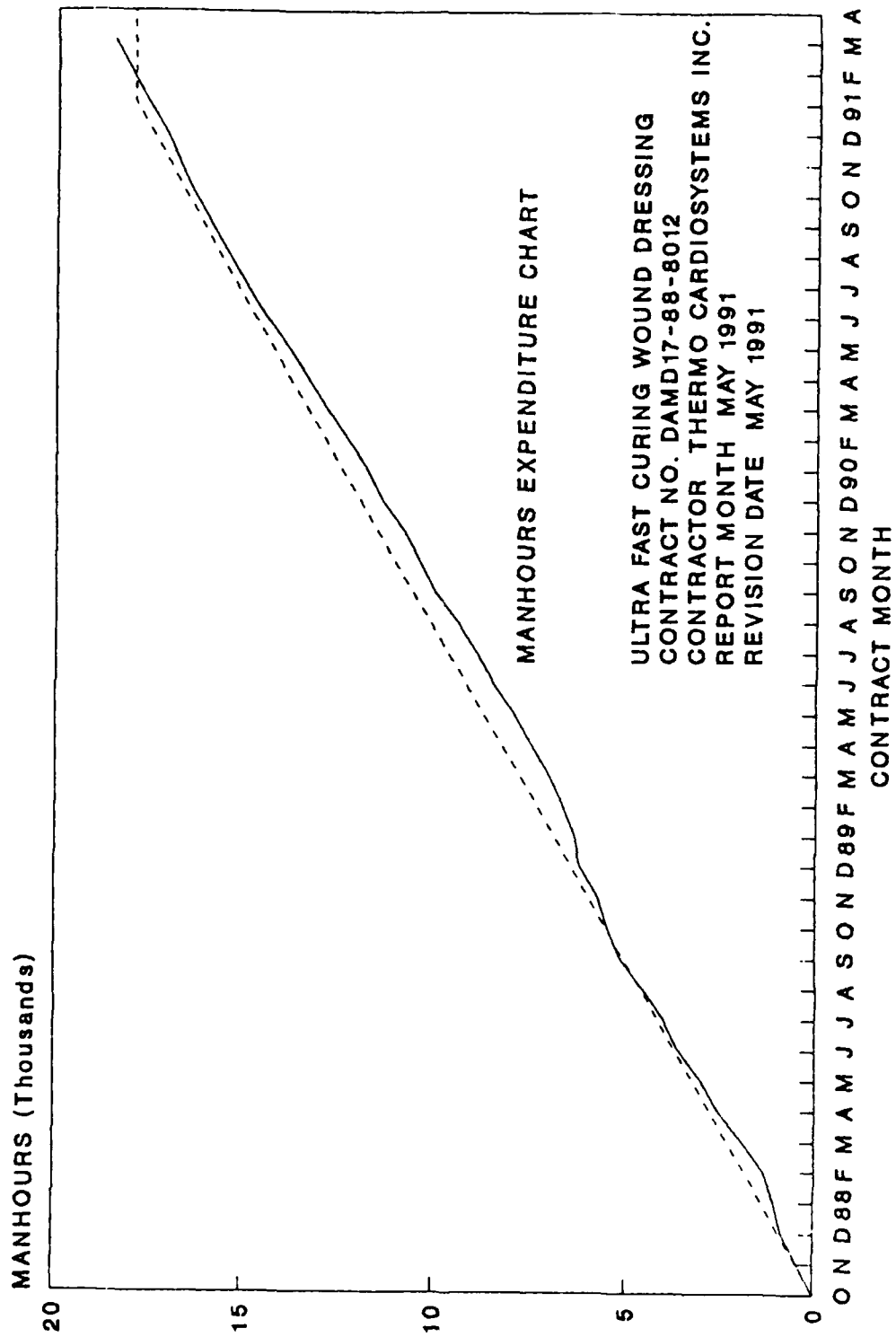


Table I. Total Labor Hours for Contract Period

	Professional		Technical	
	Required	Used	Required	Used
	11638		6340	
Dasse		90		
Szycher		188		
Lobuglio		554		
Dempsey		5986		
Thirucote		5117		
Rolfe		296		
Williams		95		
Adams				4007
Gaffney				1528
Others				650
Total	11638	12326	6340	6185

APPENDIX I

CERTIFICATE OF ANALYSIS

Thermedics Inc.

CERTIFICATE OF ANALYSIS

Antimicrobial Dermal Dressings

Date : September 4, 1990.

30% Chlorhexidine Gluconate ADD's : Batch # 008031 PDDS1

Description : A sterile 1.5 x 1.5 inch drug loaded island matrix; reinforced by a 2.5 x 2.5 inch adhesive backing, covered by a removable release liner and packaged in an aluminum pouch.

Color : White to Off-white

Thickness
total : 0.611 mm $\pm$ 0.014 mm
perimeter : 0.254 mm $\pm$ 0.013 mm.

Weight
total : 1.440 g $\pm$ 0.019 g.

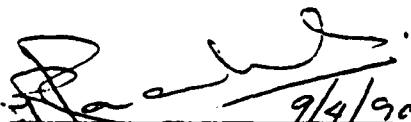
Identification : complies.
(I.R.)

Dissolution time : > 2.5 mg. per cm². in 24 hours

Biological Activity : USP XXII, 1990
P. aeruginosa positive.
S. aureus positive.

Sterility : passes
(USP XXII, 1990)

Assay : 135 mg. chlorhexidine gluconate/ADD.


Chemist 9/4/90


Manager 9/7/90

TCI

Thermo Cardiosystems Inc.

A subsidiary of Thermedics Inc. and Thermo Electron Corporation

CERTIFICATE OF ANALYSIS

Antimicrobial Dermal Dressings

Date: November 12, 1990

20% Silver sulfadiazine / 10% Chlorhexidine gluconate

Batch # 010181-PDDS2

Description : A sterile 1.5 x 1.5 inch drug loaded island matrix; reinforced by a 2.5 x 2.5 inch adhesive backing, covered by a removable release liner and packaged in an aluminum pouch.

Color : off white to cream colored

Thickness
total : 0.622 mm $\pm$ 0.014 mm
island : 0.307 mm $\pm$ 0.014 mm

Weight
total : 1.475 $\pm$ 0.34 g

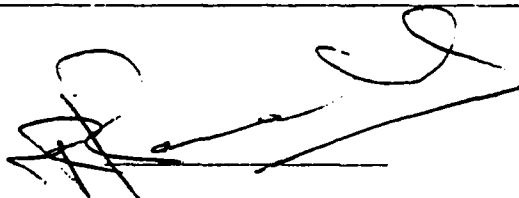
Identification : complies
(I.R.)

Dissolution time
Silver sulfadiazine : > 30 mcg per cm² in 24 hours
Chlorhexidine gluconate : > 800 mcg per cm² in 24 hours

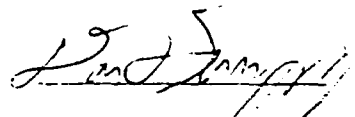
Biological activity : USP XXII, 1990
P. aeruginosa positive
S. aureus positive

Sterility : USP XXII, 1990
passes

Assay :
Chlorhexidine gluconate > 45 mg per patch



Chemist



Manager

APPENDIX II

MICROBIOLOGICAL TEST RESULTS



225 Wildwood Ave., Woburn, MA 01801
Telephone: (617) 933-6903
Fax: (617) 933-9196

TEST RESULT CERTIFICATE

Client: Thermedics, Inc.
Address: 470 Wildwood Avenue
P.O. Box 2999
Woburn, MA 01888-1799

Date of Test: 08/28/90
Test Completion: 09/04/90
P.O. #: 24156-897

Project #: 90-1835

Contact: R. Thirucote

TEST ARTICLE DESCRIPTION: Chlorhexidine Gluconate Dressing

Lot# N/A [008031-PDDS1]

t=0

NAME OF STUDY: Membrane Filtration Sterility

REFERENCE: USP XXII, 1990, Pp. 1483-1488.

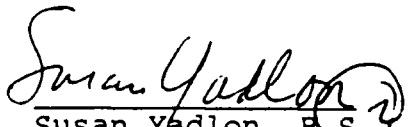
GENERAL PROCEDURE: The test articles (2 units) were aseptically pooled with 300 ml of Fluid D. The extract was then decanted into a sterile container and filtered through a sterile membrane filter. The membrane was then removed from the filter holder and cut in half. One half was immersed in 100 ml of Fluid Thioglycollate Medium (FTM) and one half was immersed in 100 ml of Trypticase Soy Broth (TSB). Each vessel was incubated at 30-35°C and 20-25°C respectively. The contents of each vessel were examined for growth during the 7 day incubation period.

RESULTS: There was no growth observed in either media inoculated with the test article during the 7 day observation period.

CONCLUSION: The test article is considered sterile according to the procedures outlined in USP XXII via membrane filtration technique.

AUTHORIZED PERSONNEL:


Steven P. Lynn, Ph.D
Study Director


Susan Yadlon, B.S.
Quality Assurance



TEST RESULT CERTIFICATE

225 Wildwood Ave., Woburn, MA 01801
Telephone: (617) 933-6903
Fax: (617) 933-9196

Client: Thermedics, Inc.
Address: 470 Wildwood Street
P.O. Box 2999
Woburn, MA 01801
Project #: 90-1836

Date of Test: 08/23/90
Test Completion: 08/27/90
P.O. #: 24139-897

Contact: R. Thirucote

TEST ARTICLE DESCRIPTION: Chlorhexidine Gluconate Dressing

LOT #: N/A [008031-PDDS1]

t=0

NAME OF STUDY: Zone of Inhibition

REFERENCE: Based on the method described in USP XXII, 1990.

GENERAL PROCEDURE: The test article was analyzed for its ability to produce a zone of inhibition against cultures of *Staphylococcus aureus* (*S. aureus*) and *Pseudomonas aeruginosa* (*P. aeruginosa*). The test article (three 0.8 cm diameter discs) and placebo discs (three 0.8 cm diameter discs) were placed on the surface of Trypticase Soy Agar containing the test organism. The positive control for *S. aureus* was a mixture of penicillin and streptomycin. The positive control for *P. aeruginosa* was ampicillin. The negative control for both organisms was an untreated filter disc. Three plates were used for each determination. The plates were inverted and incubated at 30-35°C for 72 hours.

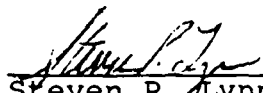
RESULTS:

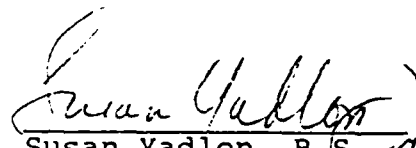
	Zone of Inhibition (in cm)							
	<i>S. aureus</i>				<i>P. aeruginosa</i>			
	1	2	3	Ave	1	2	3	Ave
Neg. Control	0	0	0	0	0	0	0	0
Pos. Control	1.40	1.30	1.30	1.33	2.0	2.0	2.0	2.0
Test Article	1.50	1.80	1.70	1.67	1.50	1.60	1.50	1.53

Toxikon Project Number 90-1836

CONCLUSION: The test article does possess antimicrobial activity against *S. aureus* and *P. aeruginosa*. The size of the zone of inhibition is indicative of antimicrobial activity, but is not a quantitative evaluation of potency as outlined in this study.

AUTHORIZED PERSONNEL:


Steven P. Lynn, Ph.D.
Study Director


Susan Yadlon, B.S.
Quality Assurance



225 Wildwood Ave., Woburn, MA 01801
Telephone: (617) 933-6903
Fax: (617) 933-9196

TEST RESULT CERTIFICATE

Client: Thermo Cardiosystems, Inc.

Date of Test: 03/13/91

Address: P.O. Box 2697
470 Wildwood Avenue
Woburn, MA 01801

Test Completion: 03/20/91

P.O. #: 3829-897

Project #: 91-0503

Contact: R. Thirucote

TEST ARTICLE DESCRIPTION: Chlorhexidine Gluconate Add's

B.N.: 008031-PDDS1

t=6M

NAME OF STUDY: Membrane Filtration Sterility

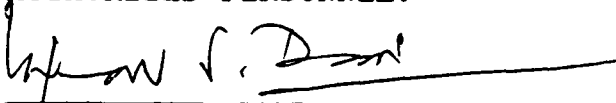
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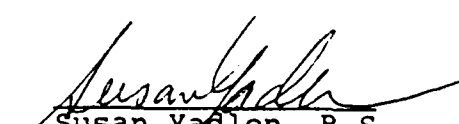
GENERAL PROCEDURE: The test articles (2 units) were aseptically pooled with 300 ml of Fluid D. The extract was then decanted into a sterile container and filtered through a sterile membrane filter. The membrane was then removed from the filter holder and cut in half. One half was immersed in 100 ml of Fluid Thioglycollate Medium (FTM) and one half was immersed in 100 ml of Trypticase Soy Broth (TSB). Each vessel was incubated at 30-35°C and 20-25°C respectively, for seven days. The contents of each vessel were examined daily for growth.

RESULTS: There was no growth observed in either media for the test article.

CONCLUSION: The test article is considered sterile according to the procedures outlined in USP XXII via membrane filtration technique.

AUTHORIZED PERSONNEL:


Laxman S. Desai, D.Sc.
Study Director


Susan Yadlon, B.S.
Quality Assurance



225 Wildwood Ave., Woburn, MA 01801
Telephone: (617) 933-6903
Fax: (617) 933-9196

TEST RESULT CERTIFICATE

Client: Thermo Cardiosystems, Inc.

Date of Test: 03/15/91

Address: 470 Wildwood Avenue

Test Completion: 03/18/91

P.O. Box 2697

P.O. #: 3829-897

Woburn, MA 01888

Project #: 91-0504

Contact: R. Thirucote

TEST ARTICLE DESCRIPTION: Chlorhexidine Gluconate Add's 30%

B.N #: 008031-PDDS1

t=6M

NAME OF STUDY: Zone of Inhibition

REFERENCE: Based on the method described in USP XXII, 1990.

GENERAL PROCEDURE: The test article was analyzed for its ability to produce a zone of inhibition against cultures of *Staphylococcus aureus* (*S. aureus*) and *Pseudomonas aeruginosa* (*P. aeruginosa*). The test article (three 0.8 cm diameter discs) and placebo discs (three 0.8 cm diameter discs) were placed on the surface of Trypticase Soy Agar (TSA) and Potatoe Dextrose Agar (PDA) containing the test organism. The positive control for *S. aureus* was a mixture of penicillin and streptomycin. The positive control for *P. aeruginosa* was ampicillin. The negative control for both organisms was an untreated filter disc. Three plates were used for each determination. The plates were inverted and incubated at 30-35°C for 72 hours.

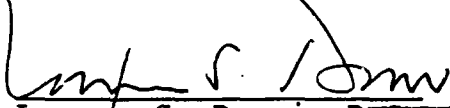
RESULTS:

Zone of Inhibition (in mm)									
	<i>S. aureus</i> (TSA)				<i>P. aeruginosa</i> (PDA)				
	1	2	3	Ave	1	2	3	Ave	
Neg. Control	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	
Pos. Control	4.5	3.7	3.7	4.0	3.8	4.1	4.0	4.0	
Test Article	2.8	2.8	2.4	2.7	2.5	2.5	2.4	2.5	

Toxikon Project Number 91-0504

CONCLUSION: The test article does possess antimicrobial activity against *S. aureus* and *P. aeruginosa*. The size of the zone of inhibition is indicative of antimicrobial activity, but is not a quantitative evaluation of potency as outlined in this study.

AUTHORIZED PERSONNEL:


Laxman S. Desai, D.Sc.
Study Director


Susan Yallon, B.S.
Quality Assurance



225 Wildwood Ave., Woburn, MA 01801
Telephone: (617) 933-6903
Fax: (617) 933-9196

TEST RESULT CERTIFICATE

Client: Thermedics, Inc.
Address: 470 Wildwood Avenue
P.O. Box 2999
Woburn, MA 01888-1799

Date of Test: 11/21/90
Test Completion: 11/28/90
P.O. #: 24801-897

Project #: 90-2152.1

Contact: R. Thirucote

TEST ARTICLE DESCRIPTION: Combination Silver Sulfadiazine/
Chlorhexidine Gluconate Dressing

Lot#: 010181-PDDS2

t=0

NAME OF STUDY: Membrane Filtration Sterility

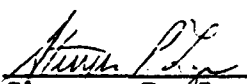
REFERENCE: USP XXII, 1990, Pp. 1483-1488.

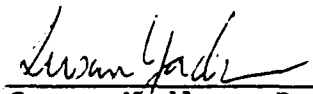
GENERAL PROCEDURE: The test articles (2 units) were aseptically pooled with 300 ml of Fluid D. The extract was then decanted into a sterile container and filtered through a sterile membrane filter. The membrane was then removed from the filter holder and cut in half. One half was immersed in 100 ml of Fluid Thioglycollate Medium (FTM) and one half was immersed in 100 ml of Trypticase Soy Broth (TSB). Each vessel was incubated at 30-35°C and 20-25°C respectively. The contents of each vessel were examined for growth during the 7 day incubation period.

RESULTS: There was no growth observed in either media inoculated with the test article during the 7 day observation period.

CONCLUSION: The test article is considered sterile according to the procedures outlined in USP XXII via membrane filtration technique.

AUTHORIZED PERSONNEL:


Steven P. Lynn, Ph.D.
Study Director


Susan Yadlon, B.S.
Quality Assurance



TEST RESULT CERTIFICATE

225 Wildwood Ave., Woburn, MA 01801
Telephone: (617) 933-6903
Fax: (617) 933-9196

Client: Thermedics, Inc.
Address: 470 Wildwood Street
P.O. Box 2999
Woburn, MA 01888
Project #: 90-2153

Date of Test: 11/26/90
Test Completion: 11/30/90
P.O. #: 24802-897

Contact: R. Thirucote

TEST ARTICLE DESCRIPTION: Combination Silver Sulfadiazine/
Chlorhexidine Gluconate Dressing

LOT #: B.N. 010181-PDDS2

t=0

NAME OF STUDY: Zone of Inhibition

REFERENCE: Based on the method described in USP XXII, 1990.

GENERAL PROCEDURE: The test article was analyzed for its ability to produce a zone of inhibition against cultures of *Staphylococcus aureus* (*S. aureus*) and *Pseudomonas aeruginosa* (*P. aeruginosa*). The test article (three 0.8 cm diameter discs) and placebo discs (three 0.8 cm diameter discs) were placed on the surface of Trypticase Soy Agar containing the test organism. The positive control for *S. aureus* was a mixture of penicillin and streptomycin. The positive control for *P. aeruginosa* was ampicillin. The negative control for both organisms was an untreated filter disc. Three plates were used for each determination. The plates were inverted and incubated at 30-35°C for 72 hours.

RESULTS:

	Zone of Inhibition (in cm)							
	S. aureus				P. aeruginosa			
	1	2	3	Ave	1	2	3	Ave
Neg. Control	0	0	0	0	0	0	0	0
Pos. Control	1.2	1.1	1.8	1.37	1.9	1.8	2.0	1.9
Test Article	1.6	1.4	1.7	1.57	1.4	1.5	1.6	1.5

Toxikon Project Number 90-2153

CONCLUSION: The test article does possess antimicrobial activity against *S. aureus* and *P. aeruginosa*. The size of the zone of inhibition is indicative of antimicrobial activity, but is not a quantitative evaluation of potency as outlined in this study.

AUTHORIZED PERSONNEL:


Steven P. Lynn, Ph.D.
Study Director


Susan Yadlon, B.S.
Quality Assurance



225 Wildwood Ave., Woburn, MA 01801
Telephone: (617) 933-6903
Fax: (617) 933-9196

TEST RESULT CERTIFICATE

Client: Thermo Cardiosystems, Inc. Technical Initiation: 05/23/91
Address: 470 Wildwood Avenue Technical Completion: 05/30/91
P.O. Box 2697 Final Report: 05/30/91
Woburn, MA 01888 P.O. #: 4120-897
Contact: R. Thirucote Project #: 91-0788

TEST ARTICLE: 20% Silver Sulfadiazine 10% Chlorhexidine
Gluconate ADDs'

Lot#: B.N 010181-PDDS2

t=6M

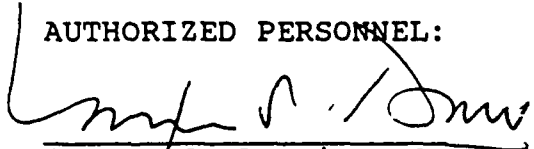
NAME OF STUDY: Membrane Filtration Sterility
REFERENCE: USP XXII, 1990

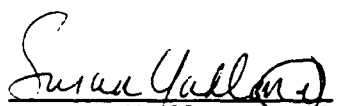
GENERAL PROCEDURE: The test articles (2 units) were aseptically pooled with 300 ml of Fluid D, decanted, and filtered through a sterile membrane filter. The membrane was removed from the filter holder and cut in half. One half was immersed in 100 ml of Fluid Thioglycollate Medium (FTM) and the other half immersed in 100 ml of Trypticase Soy Broth (TSB). Each vessel was incubated for 7 days at 30-35°C and 20-25°C, respectively. The contents of each vessel were examined for growth. One spore strip (positive control) was tested in 30 ml of TSB at 50-55°C.

RESULTS: There was no growth observed in either media for the test article. The positive control spore strip exhibited growth within 24 hours of incubation.

CONCLUSION: The test article is considered sterile according to the procedures outlined in USP XXII via membrane filtration technique.

AUTHORIZED PERSONNEL:


Laxman S. Desai, D.Sc.
Study Director


Susan Yadlon, B.S.
Quality Assurance



225 Wildwood Ave., Woburn, MA 01801
Telephone: (617) 933-6903
Fax: (617) 933-9196

TEST RESULT CERTIFICATE

Client: Thermo Cardiosystems, Inc.

Date of Test: 05/29/91

Address: 470 Wildwood Avenue
P.O. Box 2697
Woburn, MA 01888

Test Completion: 05/30/91

Report Date: 06/03/91

P.O. #: 4120-897

Project #: 91-0787

Contact: R. Thirucote

TEST ARTICLE DESCRIPTION: 20% Silver Sulfadiazine
10% Chlorhexidine Gluconate Add's

Lot #: B.N. 010181-PDDS2

t=6M

NAME OF STUDY: Zone of Inhibition

REFERENCE: Based on the method described in USP XXII, 1990.

GENERAL PROCEDURE: The test article was analyzed for its ability to produce a zone of inhibition against cultures of *Staphylococcus aureus* (*S. aureus*) and *Pseudomonas aeruginosa* (*P. aeruginosa*). The test article, cut into 0.8 cm diameter discs was placed on the surface of Medium 19 Agar containing the test organisms. The positive control was a mixture of penicillin and streptomycin. The negative control (placebo) was supplied by the Sponsor. Three plates were used for each determination. The plates were inverted and incubated at 30-35°C for 24 hours.

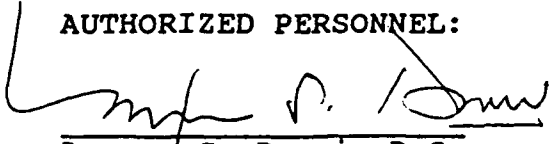
RESULTS:

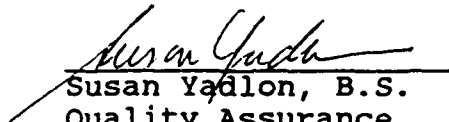
Zone of Inhibition (in mm)									
<i>S. aureus</i>					<i>P. aeruginosa</i>				
	1	2	3	Ave	1	2	3	Ave	
Neg. Control	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	
Pos. Control	3.5	2.5	4.0	3.3	3.0	5.0	2.0	3.3	
Test Article									
RT	2.5	2.5	2.0	2.3	1.5	2.0	1.5	1.7	
23°/H ₂ O	2.0	1.5	2.0	1.8	1.5	2.0	2.5	2.0	
38°/90% RH	2.0	2.0	2.5	2.2	3.5	1.5	1.5	2.2	
-40°	3.0	2.0	2.0	2.3	2.5	1.5	2.0	2.0	
45°/90% RH	1.0	3.0	1.5	1.8	2.0	2.0	1.0	1.7	

Toxikon Project Number 91-0787

CONCLUSION: The test article does possess antimicrobial activity against *S. aureus* and *P. aeruginosa*. The size of the zone of inhibition is indicative of antimicrobial activity, but is not a quantitative evaluation of potency as outlined in this study.

AUTHORIZED PERSONNEL:


Laxman S. Desai, D.Sc.
Study Director


Susan Yadlon, B.S.
Quality Assurance

APPENDIX III

IN VITRO DATA SHEETS

ELUTION RATE WORKSHEET FOR CHLORHEXIDINE GLUCONATE "A"

TITLE : Chlorhexidine Gluconate ADD's B.N. 008031E-PDSD1 (Set 1)

STANDARD CALIBRATION CURVE

= 238 nm

Data of Average Values

dil adj

mcg/ml	AUC	AUC	AVGAUC	Hr.	mcg/ml	mcg/ml	mcg/cm2	dif u/cm2
0	0	0	0	0.0	0.0	0.0	0.0	0.0
100	628592	586368	607480	0.5	434.5	434.5	1229.7	1229.7
500	2907409	2872586	2889998	1	528.0	538.9	1525.1	295.3
800	4823876	4834027	4828952	2	740.8	754.0	2133.8	608.7
1000	6348941	6321570	6335256	4	1143.6	1162.1	3288.9	1155.1
2000	13401626	12688172	13044899	8	1418.7	1447.3	4095.9	807.0
				24	1562.4	1597.9	4521.9	426.0
				48	1749.1	1788.1	5060.4	538.5
				72	1652.4	1696.1	4800.0	-260.5

Regression Output:

Constant -176096.
Std Err of Y Est 200957.1
R Squared 0.998588
No. of Observations 6
Degrees of Freedom 4

X Coefficient(s) 6537.082
Std Err of Coef. 122.9070

HR.	A cell	B cell	C cell	AVG.	STD.
0	0	0	0	0	0
0.5	2977017	2603097	2413290	2664468	234196.2
1	3493647	3103185	3230110	3275647	162625.0
2	4959537	4219846	4820048	4666477	320908.8
4	7994378	6431314	7474029	7299907	649887.7
8	9772500	8217787	9304384	9098223	651234.5
24	10647790	8783515	10680735	10037346	886694.8
48	11437887	10949407	11386142	11257812	219096.0
72	10966207	9232918	11677629	10625584	1026700.

Formulation Wt. %
Chlorhexidine 30 "After E-Beam sterilization"
Propylene Glycol 6 Set 1
PEG 300 24
Matrix 40

Date: 08/23/90
File: B008031E

ELUTION RATE WORKSHEET FOR CHLORHEXIDINE GLUCONATE "A"

TITLE : Chlorhexidine Gluconate ADD's B.N. 008031E-PDDS1 Set 2

STANDARD CALIBRATION CURVE

= 238 nm

Data of Average Values

dil adj

mcg/ml	AUC	AUC	AVGAUC	Hr.	mcg/ml	mcg/ml	mcg/cm2	dif u/cm2
0	0	0	0	0.0	0.0	0.0	0.0	0.0
100	512785	518900	515843	0.5	319.6	319.6	904.4	904.4
500	2898234	2867061	2882648	1	472.4	480.4	1359.5	455.0
800	4991913	4998578	4995246	2	601.7	613.5	1736.2	376.8
1000	5603535	5656796	5630166	4	889.3	904.3	2559.3	823.1
2000	12071584	12878013	12474799	8	1176.8	1199.1	3393.4	834.1
				24	1446.8	1476.2	4177.6	784.2
				48	1459.9	1496.0	4233.8	56.2
				72	1448.2	1484.7	4201.6	-32.2

Regression Output:

Constant -147175.
Std Err of Y Est 267615.0
R Squared 0.997240
No. of Observations 6
Degrees of Freedom 4

X Coefficient(s) 6223.124

Std Err of Coef. 163.6756

HR.	A cell	B cell	C cell	AVG.	STD.
0	0	0	0	0	0
0.5	1927035	2027821	1876734	1887554	1489223
1	3541438	2557354	2278756	2792516	541643.9
2	4585628	3276397	2929749	3597258	713067.3
4	6519381	5354612	4287108	5387033	911609.9
8	8056236	6956756	6516252	7176414	647598.1
24	3508963	8772552	3286903	8856139	502392.8
48	3385385	8640956	8786748	8937696	322110.4
72	3169720	8651421	8773646	8864929	221220.7

Formulation Wt.%
Chlorhexidine 30 "After E-Beam sterilization"
Propylene Glycol 6 Set 2
PEG 300 24
Matrix 40

Date: 08/27/90
File: E0080312.WK1

ELUTION RATE WORKSHEET FOR CHLORHEXIDINE GLUCONATE "A"

TITLE : Chlorhexidine Gluconate ADD's B.N. 008031-PDDS1 2 Month Sample @ 45 C/ 90% RH

STANDARD CALIBRATION CURVE

= 238 nm

Data of Average Values

dil adj

mcg/ml	AUC	AUC	AVGAUC	Hr.	mcg/ml	mcg/ml	mcg/cm2	dif u/cm2
0	0	0	0	0.0	0.0	0.0	0.0	0.0
100	467687	448195	457941	0.5	334.0	334.0	945.2	945.2
500	3040010	2886689	2963350	1	496.0	504.4	1427.3	482.2
800	4782207	4784922	4783565	2	520.1	532.5	1506.9	79.6
1000	5675335	5459266	5567301	4	717.3	730.3	2066.8	559.9
2000	12726955	12585654	12656305	8	974.5	992.4	2808.5	741.7
				24	1305.9	1330.3	3764.7	956.2
				48	1364.7	1397.4	3954.6	189.9
				72	1440.4	1474.5	4172.8	218.2

Regression Output:

Constant	-218372.	2 MONTH STABILITY
Std Err of Y Est	313113.3	45 C/90% RH
R Squared	0.996322	
No. of Observations	6	
Degrees of Freedom	4	

X Coefficient(s) 6304.249

Std Err of Coef. 191.5027

HR.	A cell	B cell	C cell	AVG.	STD.
0	0	0	0	0	0
0.5	1776137	1767078	1752691	1655524	2206288
1	2501919	2605821	3618084	2164971	1887114.
2	2601741	3002645	3576465	3060283.	215059.8
4	3260297	4336471	5314697	4303821.	2908608
8	5348750	5605877	6820239	5924955.	503465.3
24	7974299	7664704	8404695	8014566	400011.1
48	8425247	7619909	9110626	8385260.	839022.9
72	8438032	7722994	10425168	8862064.	641705.1

Formulation	Wt.%	Date:	10/29/90
Chlorhexidine	30	File:	2MSTA-45
Propylene Glycol	6		
PEG 300	24		
Matrix	40		

ELUTION RATE WORKSHEET FOR CHLORHEXIDINE GLUCONATE "A"

TITLE : Chlorhexidine Gluconate ADD's B.N. 008031-PDDSI 2 Month Sample @ 38 C/90% RH

STANDARD CALIBRATION CURVE

= 238 nm

Data of Average Values

mcg/ml	AUC	AUC	AVGAUC	Hr.	mcg/ml	mcg/ml	mcg/cm2	dif u/cm2
0	0	0	0	0.0	0.0	0.0	0.0	0.0
100	626401	622783	624592	0.5	303.2	303.2	858.0	858.0
500	3037933	3021214	3029574	1	453.1	460.7	1303.8	445.8
800	5340031	5204862	5272447	2	583.1	594.5	1682.3	378.5
1000	6333264	6046154	6189709	4	879.3	893.8	2529.6	847.3
2000	11743334	11517463	11630399	8	1172.3	1194.3	3379.9	850.3
				24	1397.1	1426.4	4036.7	656.9
				48	1386.0	1420.9	4021.3	-15.4
				72	1398.4	1433.1	4055.7	34.4

Regression Output:

Constant	169858.1	2 MONTH STABILITY
Std Err of Y Est	280538.4	38 C/90% RH
R Squared	0.996567	
No. of Observations	6	
Degrees of Freedom	4	

X Coefficient(s) 5847.175

Std Err of Coef. 171.5796

HR.	A cell	B cell	C cell	AVG.	STD.
0	0	0	0	0	0
0.5	2125830	2117694	1848705	1728560	1911143
1	2620294	3031225	2806785	2819434	168000.1
2	3363007	3721117	3654393	3579505	155492.2
4	4953856	5162431	5816949	5311078	387699.5
8	6677589	6931111	7465099	7024599	328225.6
24	3017622	3383899	3615243	3338921	246041.9
48	8108139	8615774	8098531	8274148	241597.9
72	3296233	3274380	3462823	3346812	87438.23

Formulation Wt.%
 Chlorhexidine 30
 Propylene Glycol 6
 PEG 300 24
 Matrix 40

Date: 10/31/90
 File: 2MSTA-38.WK1

ELUTION RATE WORKSHEET FOR CHLORHEXIDINE GLUCONATE "A"

TITLE : Chlorhexidine Gluconate ADD's B.N. 008031-PDDS1 2 Month Sample @ RT

STANDARD CALIBRATION CURVE

= 238 nm

Data of Average Values

mcg/ml	AUC	AUC	AVGAUC	Hr.	dil adj			
					mcg/ml	mcg/ml	mcg/cm2	diff/cm2
0	0	0	0	0.0	0.0	0.0	0.0	0.0
500	3226522	3096717	3161620	0.5	377.6	377.6	1068.6	1068.6
800	5019617	5236543	5128080	1	537.0	546.5	1546.5	477.9
1000	6157377	6295124	6226251	2	617.4	630.8	1785.3	238.8
2000	12265064	12565648	12415356	4	924.8	940.3	2661.0	375.7
				8	1292.7	1315.8	3723.7	1062.7
				24	1606.9	1639.2	4638.9	915.2
				48	1671.0	1711.2	4842.6	203.7
				72	1699.7	1741.5	4928.4	85.8

Regression Output:

Constant 58610.99
Std Err of Y Est 77878.70
R Squared 0.999783
No. of Observations 5
Degrees of Freedom 3

2 MONTH STABILITY
ROOM TEMPERATURE

X Coefficient(s) 6194.942
Std Err of Coef. 52.60153

HR.	A cell		B cell		C cell		AVG.	STD.
0	0	0	0	0	0	0	0	0
0.5	2279151	2276466	2357840	2254422	2663956	2554740	2397762.	156217.1
1	3026535		3761713		3368010		3385419.	300387.5
2	3594926		4425371		3630063		3883453.	383462.0
4	5079486		6632755		5651642		5787961	641403.8
8	7827790		9056229		7315886		8066635	730289.2
24	10302011		10737379		8999629		10013006	738280.2
48	9549833		10528555		11152494		10410294	659605.8
72	12435010		10346774		8982704		10588162	1419696.

Formulation Wt.%
Chlorhexidine 30
Propylene Glycol 6
PEG 300 24
Matrix 40

Date: 11/1/90
File: ZMSTA-RT.WK1

ELUTION RATE WORKSHEET FOR CHLORHEXIDINE GLUCONATE "A"

TITLE : Chlorhexidine Gluconate ADD's B.N. 008031-PDDS1 2 Month Sample @ RT Under Water

STANDARD CALIBRATION CURVE

= 238 nm

Data of Average Values

dil adj

mcg/ml	AUC	AUC	AVCAUC	Hr.	mcg/ml	mcg/ml	mcg/cm2	dil u/cm2
0	0	0	0	0.0	0.0	0.0	0.0	0.0
100	626401	622783	624592	0.5	414.5	414.5	1173.0	1173.0
500	3037933	3021214	3029574	1	529.7	540.1	1528.5	355.5
800	5340031	5204862	5272447	2	676.0	689.2	1950.5	422.0
1000	6333264	6046154	6189709	4	1053.2	1070.1	3028.3	1077.7
2000	11743334	11517463	11630399	8	1434.4	1460.8	4133.9	1105.6
				24	1668.4	1704.3	4823.1	689.2
				48	1704.0	1745.7	4940.4	117.3
				72	1729.1	1771.7	5013.9	73.5

Regression Output:

Constant	169858.1	2 MONTH STABILITY
Std Err of Y Est	280538.4	23 C UNDER WATER
R Squared	0.996567	
No. of Observations	6	
Degrees of Freedom	4	

X Coefficient(s) 5847.175
Std Err of Coef. 171.5796

HR.	A cell	B cell	C cell	AVG.	STD.
0	0	0	0	0	0
0.5	2424855	2323061	3118498	3246501	2276840
1	3080080	3597024	3125047	2171426	2593530
2	3994260	4393172	3980116	4122516	424662.9
4	6684914	5969763	6328969	8557174	233812.7
8	9068202	8059535	8543785	6327882	191469.7
24	10040597	9885297	9850336	8557174	291960.1
48	10597998	9603919	10198670	3925410	411895.3
72	10488406	10328725	10023552	10133529	32690.59
				10280227	408436.6
					192849.3

Formulation Wt. %
Chlorhexidine 30
Propylene Glycol 6
PEG 300 24
Matrix 40

Date: 10/31/90
File: ZMSTA-RW.WK1

ELUTION RATE WORKSHEET FOR CHLORHEXIDINE GLUCONATE "A"

TITLE : Chlorhexidine Gluconate ADD's B.N. 008031-PDDS1 2 Month Sample @ -40 C

STANDARD CALIBRATION CURVE

= 238 nm

Data of Average Values

dil adj

mcg/ml	AUC	AUC	AVGAUC	Hr.	mcg/ml	mcg/ml	mcg/cm2	dil u/cm2
0	0	0	0	0.0	0.0	0.0	0.0	0.0
100	626401	622783	624592	0.5	429.8	429.8	1216.3	1216.3
500	3037933	3021214	3029574	1	579.5	590.3	1670.5	454.3
800	5340031	5204862	5272447	2	705.4	719.9	2037.3	366.8
1000	6333264	6046154	6189709	4	1079.2	1096.8	3104.1	1066.7
2000	11974791	12439009	12206900	8	1425.4	1452.4	4110.2	1006.1
				24	1595.5	1631.1	4616.1	505.9
				48	1711.7	1751.6	4957.0	340.9
				72	1597.5	1640.3	4642.1	-314.9

Regression Output:

Constant	65627.83	2 MONTH STABILITY
Std Err of Y Est	175155.4	-40 C
R Squared	0.998776	
No. of Observations	6	
Degrees of Freedom	4	

X Coefficient(s) 6120.330

Std Err of Coef. 107.1265

HR.	A cell	B cell	C cell	AVG.	STD.
0	0	0	0	0	0
0.5	3005261	3001797	2907659	2908428	2188405
1	3747506	3869550	3220932	2164476	2696004
2	4208834	4393063	4546986	2696004	369515.4
4	7330400	6343106	6338632	3612662	281440.7
8	8921695	9107754	8338855	4382961	138234.6
24	10259998	9456351	9775574	5670712	466472.9
48	11104808	9901390	10619253	8789434	327537.2
72	10357488	9353494	9817888	3830641	330390.0
				10541817	494335.2
				9842956	410261.9

Formulation Wt. %
 Chlorhexidine 30
 Propylene Glycol 6
 PEG 300 24
 Matrix 40

Date: 10/30/90
 File: 2MSTA-40.WK1

ELUTION RATE WORKSHEET FOR CHLORHEXIDINE GLUCONATE "A"

TITLE : Chlorhexidine Gluconate ADD's B.N. 008031-PDDS1 4 Month Sample @ 45 C/ 90% RH

STANDARD CALIBRATION CURVE

= 238 nm

Data of Average Values

dil adj

mcg/ml	AUC	AUC	AVGAUC	Hr.	mcg/ml	mcg/ml	mcg/cm2	dif u/cm2
0	0	0	0	0.0	0.0	0.0	0.0	0.0
100	483774	496960	490367	0.5	286.1	286.1	809.7	809.7
500	3175808	3019575	3097692	1	403.3	410.5	1161.6	352.0
800	4972109	5073741	5022925	2	457.9	468.0	1324.4	162.3
1000	6270407	6372312	6321360	4	674.8	686.2	1942.0	617.6
2000	12105367	11985874	12045621	8	846.6	863.4	2443.6	501.6
				24	1135.2	1156.4	3272.5	828.9
				48	1199.1	1227.5	3473.7	201.2
				72	1195.3	1225.3	3467.6	-6.1

Regression Output:

Constant 40097.48 4 MONTH STABILITY
 Std Err of Y Est 162188.6 45 C/90% RH
 R Squared 0.998935
 No. of Observations 6
 Degrees of Freedom 4

X Coefficient(s) 6076.676

Std Err of Coef. 99.19593

HR.	A cell	B cell	C cell	AVG.	STD.
0	0	0	0	0	0
0.5	1659118	1640331	2160768	2034666	1582085
1	2322659	2829765	2320176	2490866	239639.4
2	2553272	3137565	2777239	2822692	240692.1
4	3626457	4452011	4342995	4140487	366189.1
8	4342395	4975944	6234537	5184492	786173.0
24	5947486	7312381	7555092	6938319	707597.1
48	6120063	7475092	8384355	7326503	930345.2
72	6170239	7741562	7969198	7303686	808298.2

Formulation Wt.%
 Chlorhexidine 30
 Propylene Glycol 6
 PEG 300 24
 Matrix 40

Date: 01/02/91
 File: 4MSTA-45

ELUTION RATE WORKSHEET FOR CHLORHEXIDINE GLUCONATE "A"

TITLE : Chlorhexidine Gluconate ADD's B.N. 008031-PDDS1 4 Month Sample @ 38 C/ 90% R.H.

STANDARD CALIBRATION CURVE

= 238 nm

Data of Average Values

dil adj

mcg/ml	AUC	AUC	AVG AUC	Hr.	mcg/ml	mcg/ml	mcg/cm2	dif u/cm2
0	0	0	0	0.0	0.0	0.0	0.0	0.0
100	483774	496960	490367	0.5	246.0	246.0	696.1	696.1
500	3175808	3019575	3097692	1	437.4	443.5	1255.1	559.1
800	4972109	5073741	5022925	2	580.2	591.2	1673.0	417.9
1000	6270407	6372312	6321360	4	732.9	747.4	2115.1	442.0
2000	12105367	11985874	12045621	8	1109.7	1128.0	3192.2	1077.1
				24	1315.9	1343.7	3802.6	610.4
				48	1458.9	1491.8	4221.9	419.3
				72	1409.3	1445.8	4091.5	-139.4

Regression Output:

Constant	40097.48	4 MONTH STABILITY
Std Err of Y Est	162188.6	38 C/90% RH
R Squared	0.998935	
No. of Observations	6	
Degrees of Freedom	4	

X Coefficient(s) 6076.676

Std Err of Coef. 99.19593

HR.	A cell	B cell	C cell	AVG.	STD.
0	0	0	0	0	0
0.5	1555953	1522395	1577638	1642328	1422335
1	2699292	3022119	2372003	2697804	265410.8
2	3420408	3741443	3536285	3566045	132740.6
4	5193744	4224488	4062155	4493462	499589.0
8	7064453	6485492	6799499	6783150	236644.8
24	3873812	7300184	7435609	3036535	610466.1
48	10998284	7981894	7736483	8905553	1483171.
72	8239171	10233255	7339333	8603919	1209263.

Formulation Wt.%
 Chlorhexidine 30
 Propylene Glycol 6
 PEG 300 24
 Matrix 40

Date: 01/02/91
 File: 4MSTA-38.WK1

ELUTION RATE WORKSHEET FOR CHLORHEXIDINE GLUCONATE "A"

TITLE : Chlorhexidine Gluconate ADD's B.N. 008031-PDDS1 4 Month Sample @ RT

STANDARD CALIBRATION CURVE

= 238 nm

Data of Average Values

dil adj

mcg/ml	AUC	AUC	AVGAUC	Hr.	mcg/ml	mcg/ml	mcg/cm2	dil u/cm2
0	0	0	0	0.0	0.0	0.0	0.0	0.0
100	483774	496960	490367	0.5	400.6	400.6	1133.6	1133.6
500	3175808	3019575	3097692	1	493.0	503.0	1423.5	289.2
800	4972109	5073741	5022925	2	651.8	664.1	1879.4	455.9
1000	6270407	6372312	6321360	4	329.4	945.7	2676.3	796.9
2000	12105367	11985874	12045621	8	1414.9	1438.2	4070.0	1393.7
				24	1530.8	1566.2	4432.4	362.4
				48	1572.0	1610.2	4557.0	124.6
				72	1623.7	1663.0	4706.4	149.4

Regression Output:

Constant	40097.48	4 MONTH STABILITY
Std Err of Y Est	162188.6	ROOM TEMPERATURE
R Squared	0.998935	
No. of Observations	6	
Degrees of Freedom	4	

X Coefficient(s) 6076.676

Std Err of Coef. 99.19593

HR.	A cell	B cell	C cell	AVG.	STD.
0	0	0	0	0	0
0.5	2475505	2579576	2786440	2797086	2099471
1	3100808	3013634	2992924	2107149	2474204
2	3814916	4263113	3924233	4000754	285190.9
4	5467471	6474483	5121392	5687782	46746.55
8	9389366	8761175	7763876	8638139	190808.3
24	9243781	10087644	8636030	9342485	573943.3
48	9218143	9297848	10261347	9592448	669282.1
72	9229983	11739188	8751998	9907056	572395.1
					474100.8
					1310126.

Formulation Wt.%
Chlorhexidine 30
Propylene Glycol 6
PEG 300 24
Matrix 40

Date: 01/03/91
File: 4MSTA-RT.WK1

ELUTION RATE WORKSHEET FOR CHLORHEXIDINE GLUCONATE "A"

TITLE : Chlorhexidine Gluconate ADD's B.N. 008031-PDDS1 4 Month Sample @ RT Under Water

STANDARD CALIBRATION CURVE

= 238 nm

Data of Average Values

dil adj

mcg/ml	AUC	AUC	AVGAUC	Hr.	mcg/ml	mcg/ml	mcg/cm2	dil u/cm2
0	0	0	0	0.0	0.0	0.0	0.0	0.0
100	483774	496960	490367	0.5	365.5	365.5	1034.3	1034.3
500	3175808	3019575	3097692	1	495.7	504.8	1428.7	394.4
800	4972109	5073741	5022925	2	677.8	690.2	1953.2	524.5
1000	6270407	6372312	6321360	4	905.5	922.5	2610.6	657.4
2000	12105367	11985874	12045621	8	1324.3	1346.9	3811.8	1201.3
				24	1572.0	1605.1	4542.6	730.7
				48	1680.4	1719.7	4866.7	324.1
				72	1661.8	1703.8	4821.8	-44.0

Regression Output:

Constant	40097.48	4 MONTH STABILITY
Std Err of Y Est	162188.6	23 C UNDER WATER
R Squared	0.998935	
No. of Observations	6	
Degrees of Freedom	4	

X Coefficient(s) 6076.676

Std Err of Coef. 99.19593

HR.	A cell	B cell	C cell	AVG.	STD.
0	0	0	0	0	0
0.5	2138547	2110351	2569691	2534382	2088199
1	2925105	3463422	2768320	3052282	297682.4
2	4115787	4301791	4058718	4158765	103783.3
4	5810866	5596235	5220913	5542671	243807.2
8	8192582	7385759	8084056	8087465	84469.55
24	3677755	9216571	9884328	3592884	279138.0
48	11125597	9588555	10039492	10251214	645106.9
72	10829619	3539690	10045546	10138285	530678.5

Formulation Wt.%
 Chlorhexidine 30
 Propylene Glycol 6
 PEG 300 24
 Matrix 40

Date: 01/02/91
 File: 4MSTA-RW.WK1

ELUTION RATE WORKSHEET FOR CHLORHEXIDINE GLUCONATE "A"

TITLE : Chlorhexidine Gluconate ADD's B.N. 008031-PDDS1 4 Month Sample @ - 40 C

STANDARD CALIBRATION CURVE

= 238 nm

				Data of Average Values			
				dil adj			
mcg/ml	AUC	AUC	AVGAUC	Hr.	mcg/ml	mcg/ml	mcg/cm2 dif u/cm2
0	0	0	0	0.0	0.0	0.0	0.0
100	483774	496960	490367	0.5	385.4	385.4	1090.6
500	3175808	3019575	3097692	1	571.0	580.6	1643.1
800	4972109	5073741	5022925	2	735.5	749.7	2121.8
1000	6270407	6372312	6321360	4	1081.3	1099.7	3112.2
2000	12105367	11985874	12045621	8	1430.0	1457.0	4123.5
				24	1686.8	1722.5	4874.7
				48	1697.3	1739.4	4922.6
				72	1590.3	1632.7	4620.6

Regression Output:

Constant 40097.48 4 MONTH STABILITY
Std Err of Y Est 162188.6 -40 C
R Squared 0.998935
No. of Observations 6
Degrees of Freedom 4

X Coefficient(s) 6076.676
Std Err of Coef. 99.19593

HR.	A cell	B cell	C cell	AVG.	STD.
0	0	0	0	0	0
0.5	2130814	2121731	2378740	2518736	2596571
1	3382603	3682870	3463445	3509639	126860.8
2	4473437	4525618	4528844	4509299	25392.91
4	6448878	6382939	7000937	6610918	277095.7
8	8096432	9427615	8665500	8729849	545354.7
24	9960974	11171996	9737083	10290017	630315.3
48	9600819	12107873	3353078	10353923	1244346.
72	9313029	10725875	3072647	3703850.	729313.2

Formulation Wt.%
Chlorhexidine 30
Propylene Glycol 6
PEG 300 24
Matrix 40

Date: 01/02/91
File: 4MSTA-40.WK1

ELUTION RATE WORKSHEET FOR CHLORHEXIDINE GLUCONATE "A"

TITLE : Chlorhexidine Gluconate ADD's B.N. 008031-PDDS1 6 Month Sample @ 45 C/90% RH

STANDARD CALIBRATION CURVE

= 238 nm

Data of Average Values

dil adj

mcg/ml	AUC	AUC	AVCAUC	Hr.	mcg/ml	mcg/ml	mcg/cm2	dil u/cm2
0	0	0	0	0.0	0.0	0.0	0.0	0.0
100	468111	466557	467334	0.5	256.3	256.3	725.2	725.2
500	2197937	2153838	2178888	1	398.0	401.9	1137.3	412.1
800	3823419	3861757	3842588	2	475.7	481.6	1363.1	225.8
1000	4786595	4731125	4758860	4	568.1	575.3	1628.0	265.0
2000	11213550	11120588	11167069	8	858.0	866.5	2452.3	824.3
				24	1226.4	1239.3	3507.2	1054.9
				48	1374.6	1393.0	3942.2	435.0
				72	1310.9	1331.5	3768.3	-173.9

Regression Output:

Constant -342102. 6 MONTH STABILITY
 Std Err of Y Est 412264.6 45 C/90% RH
 R Squared 0.991842
 No. of Observations 6
 Degrees of Freedom 4

X Coefficient(s) 5560.762
 Std Err of Coef. 352.1445

HR.	A cell	B cell	C cell	AVG.	STD.
0	0	0	0	0	0
0.5	1009789	996879	1043022	1032641	1170294
1	1574676	1949058	2090036	1871256	217468.4
2	1676694	2379839	2852522	2303018	483093.4
4	1977629	3689380	2784457	2817155	699201.8
8	2601752	5205182	5480242	4429058	1296971.
24	4911387	6359730	7562015	6477710	1134523.
48	6701965	7087593	8115738	7301765	596708.1
72	6471697	7527608	6843511	6947605	437312.8

Formulation Wt.%
 Chlorhexidine 30
 Propylene Glycol 6
 PEG 300 24
 Matrix 40

Date: 02/26/91
 File: 6MSTA-45.WK1

ELUTION RATE WORKSHEET FOR CHLORHEXIDINE GLUCONATE "A"

TITLE : Chlorhexidine Gluconate ADD's B.N. 008031-PDDS1 6 Month Sample @ 38 C/90% RH

STANDARD CALIBRATION CURVE

= 238 nm

				Data of Average Values			
				dil adj			
mcg/ml	AUC	AUC	AVGAUC	Hr.	mcg/ml	mcg/ml	mcg/cm2 dif u/cm2
0	0	0	0	0.0	0.0	0.0	0.0
100	468111	466557	467334	0.5	383.0	383.0	1084.0
500	2197937	2159838	2178888	1	466.1	471.8	1335.3
800	3823419	3861757	3842588	2	557.2	564.2	1596.6
1000	4786595	4731125	4758860	4	787.6	796.0	2252.6
2000	11213550	11120588	11167069	8	1122.6	1134.4	3210.4
				24	1348.7	1365.6	3864.5
				48	1289.5	1309.7	3706.5
				72	1515.3	1534.6	4342.9

Regression Output:

Constant	-342102.	6 MONTH STABILITY
Std Err of Y Est	412264.6	38 C/90% RH
R Squared	0.991842	
No. of Observations	6	
Degrees of Freedom	4	

X Coefficient(s) 5560.762
Std Err of Coef. 252.1445

HR.	A cell	B cell	C cell	AVG.	STD.
0	0	0	0	0	0
0.5	2032165	2223901	1677148	1760453	1469470
1	2266486	2401124	2981271	2249637	131122.4
2	3352777	2469674	2446307	2756252	421914.2
4	4892261	3446749	3774163	4037724	518856.2
8	6747489	5254448	5699426	5900454	625887.1
24	7484229	7379074	6610054	7157785	389676.6
48	7412122	7007982	6065073	6828392	564402.0
72	3202462	7964303	7084958	3083907	868594.5

Formulation Wt.%
Chlorhexidine 30
Propylene Glycol 5
PEG 300 24
Matrix 40

Date: 02/28/91
File: GMSTA-38.WK1

ELUTION RATE WORKSHEET FOR CHLORHEXIDINE GLUCONATE "A"

TITLE : Chlorhexidine Gluconate ADD's B.N. 008031-PDDSI 6 Month Sample @ RGT

STANDARD CALIBRATION CURVE

= 238 nm

				Data of Average Values			
				dil adj			
mcg/ml	AUC	AUC	AVGAUC	Hr.	mcg/ml	mcg/ml	mcg/cm2 dif u/cm2
0	0	0	0	0.0	0.0	0.0	0.0
100	468111	466557	467334	0.5	415.7	415.7	1176.4
500	2197937	2159838	2178888	1	558.4	564.6	1597.9
800	3823419	3861757	3842588	2	718.4	726.7	2056.7
1000	4786595	4731125	4758860	4	1007.1	1017.9	2880.5
2000	11213550	11120588	11167069	8	1369.3	1384.4	3917.8
				24	1719.3	1740.4	4925.4
				48	1761.6	1787.4	5058.3
				72	1669.1	1695.6	4798.5

Regression Output:

Constant	-342102.	6 MONTH STABILITY
Std Err of Y Est	412264.6	ROOM TEMPERATURE
R Squared	0.991842	
No. of Observations	6	
Degrees of Freedom	4	

X Coefficient(s) 5560.762

Std Err of Coef. 252.1445

HR.	A cell	B cell	C cell	AVG.	STD.
0	0	0	0	0	0
0.5	2015344	2196492	1888163	1801489	1919087
1	2469263	2549557	3270177	1995582	1969359
2	3707421	3629135	3621104	3652553	38935.58
4	5161096	5147881	5465163	5258046	146552.6
8	7328602	7107940	7379882	7272141	117980.1
24	9686430	8372149	9606579	3221719	501620.7
48	8871077	10295870	9194121	9453689	609940.1
72	8343151	9230042	9245659	8939619	421815.1

Formulation Wt. %
 Chlorhexidine 30
 Propylene Glycol 6
 PEG 300 24
 Matrix 40

Date: 03/08/91
 File: GMSTA-RT.WK1

ELUTION RATE WORKSHEET FOR CHLORHEXIDINE GLUCONATE "A"

TITLE : Chlorhexidine Gluconate ADD's B.N. 008031-PDDS1 6 Month Sample @ 2T/WATER

STANDARD CALIBRATION CURVE

= 238 nm

				Data of Average Values				
				dil adj				
mcg/ml	AUC	AUC	AVGAUC	Hr.	mcg/ml	mcg/ml	mcg/cm2	diff/cm2
0	0	0	0	0.0	0.0	0.0	0.0	0.0
100	468111	466557	467334	0.5	341.5	341.5	966.4	966.4
500	2197937	2159838	2178888	1	606.7	611.9	1731.5	765.2
800	3823419	3861757	3842588	2	743.4	752.5	2129.6	398.1
1000	4786595	4731125	4758860	4	1052.6	1063.8	3010.5	880.9
2000	11213550	11120588	11167069	8	1619.7	1635.4	4628.3	1617.8
				24	1868.9	1893.2	5357.8	729.5
				48	2117.9	2146.0	6073.1	715.3
				72	2043.9	2075.7	5874.1	-199.0

Regression Output:

Constant	-342102.	6 MONTH STABILITY
Std Err of Y Est	412264.6	23 CUNDER WATER
R Squared	0.391842	
No. of Observations	6	
Degrees of Freedom	4	

X Coefficient(s) 5560.762
Std Err of Coef. 252.1445

HR.	A cell		B cell		C cell		AVG.	STD.
0	0	0	0	0	0	0	0	0
0.5	1092069	1132431	1819236	1824720	1824720	1601975	1556790	318902.3
1	2833779		3073257		3188331		3031789	147685.4
2	3964774		3521818		3888913		3791835	193426.3
4	5288056		5136404		5109667		5511375	427562.0
8	8179055		10024860		7789272		8664395	375065.8
24	3833503		13004202		7253864		10050523	2350189.
48	10569555		12296671		11439417		11435214	705098.4
72	11621978		10588402		10859959		11023446	437504.9

Formulation Wt.%
Chlorhexidine 30
Propylene Glycol 6
PEG 300 24
Matrix 40

Date: 02/28/91
File: 6MSTA-RW.WK1

ELUTION RATE WORKSHEET FOR CHLORHEXIDINE GLUCONATE "A"

TITLE : Chlorhexidine Gluconate ADD's B.N. 008031-PDOS1 6 Month Sample @ - 40 C

STANDARD CALIBRATION CURVE

= 238 nm

Data of Average Values

dil adj

mcg/ml	AUC	AUC	AVGAUC	Hr.	mcg/ml	mcg/ml	mcg/cm2	dil a/cm2
0	0	0	0	0.0	0.0	0.0	0.0	0.0
100	468111	466557	467334	0.5	462.7	462.7	1309.4	1309.4
500	2197937	2159838	2178888	1	588.5	595.4	1685.0	375.6
800	3823419	3861757	3842588	2	709.6	718.5	2033.2	348.3
1000	4786595	4731125	4758860	4	981.8	992.4	2808.6	775.3
2000	11213550	11120588	11167069	8	1275.1	1289.8	3650.1	841.5
				24	1524.7	1553.9	4397.4	747.4
				48	1560.8	1583.9	4482.3	84.9
				72	1758.0	1781.4	5041.5	559.1

Regression Output:

Constant -342102. 6 MONTH STABILITY
 Std Err of Y Est 412264.6 -40 C
 R Squared 0.991842
 No. of Observations 6
 Degrees of Freedom 4

X Coefficient(s) 5560.762
 Std Err of Coef. 252.1445

HR.	A cell	B cell	C cell	AVG.	STD.
0	0	0	0	0	0
0.5	2349318	2259408	2360281	2405449	1977451
1	2822315	3298349	2669804	2930156	267693.1
2	3673438	4323118	2815447	3604001	617459.3
4	5500934	6121526	3729713	5117391	1013417.
8	7509981	7264724	5469863	6742189.	309441.7
24	8395600	3653446	7527666	8192237.	481568.5
48	8934111	7885349	8192598	3337352.	440220.2
72	9119582	10613321	8562564	3433822.	863835.6

Formulation Wt. %
 Chlorhexidine 30
 Propylene Glycol 6
 PEG 300 24
 Matrix 40

Date: 02/26/91
 File: SMSTA-40.WK1

ELUTION RATE WORKSHEET FOR SILVER SULFADIAZINE "A"

TITLE : 20:10 Silver sulfadiazine:Chlorhexidine Gluconate ADD's B.N. 010181-PDDS2 Set 1

STANDARD CALIBRATION CURVE

= 254 nm

				Data of Average Values				
				dil adj				
mcg/ml	AUC	AUC	AVGAUC	Hr.	mcg/ml	mcg/ml	mcg/cm2	dif $\pm$ /cm2
0	0	0	0	0.0	0.0	0.0	0.0	0.0
1	47448	49730	48614	0.5	2.9	2.9	8.3	8.3
5	281594	286471	284033	1	4.2	4.3	12.1	3.8
10	568117	576598	572358	2	6.4	6.5	18.3	6.1
15	833426	847205	840316	4	9.2	9.4	26.6	8.3
				8	11.2	11.5	32.5	5.9
				24	12.2	12.4	35.2	2.8
				48	14.0	14.3	40.5	5.3
				72	13.8	14.2	40.0	-0.5

Regression Output:

Constant -1388.48
 Std Err of Y Est 7360.972
 R Squared 0.999679
 No. of Observations 5
 Degrees of Freedom 3

X Coefficient(s) 56524.57
 Std Err of Coef. 584.1305

HR.	A cell	B cell	C cell	AVG.	STD.
0	0	0	0	0	0
0.5	172125	162597	160724	165148.6	4991.923
1	232953	251906	226010	236358.3	10943.53
2	354554	360935	358230	357906.3	2615.066
4	523156	510231	526826	520071	7117.416
8	649196	675252	577233	633893.6	41453.20
24	694514	703979	659998	686163.6	18901.11
48	837370	741313	792565	790416	39244.53
72	759865	815255	760980	778700	25852.29

Formulation Wt.%
 Silver sulfadiazine 20
 Chlorhexidine gluconate 10
 Pluronic L-62 20
 Matrix 50

Date: 11/26/90
 File: SD101811.WK1

ELUTION RATE WORKSHEET FOR CHLORHEXIDINE GLUCONATE "A"

TITLE : 20:10 Silver Sulfadiazine:Chlorhexidine Gluconate ADD's B.N. 010181-PPDS2 Set 1

STANDARD CALIBRATION CURVE

= 238 nm

				Data of Average Values			
				dil adj			
mcg/ml	AUC	AUC	AVGAUC	Hr.	mcg/ml	mcg/ml	mcg/cm2 dif u/cm2
0	0	0	0	0.0	0.0	0.0	0.0
100	655604	501975	578790	0.5	110.1	110.1	311.6
500	2989292	3056439	3022866	1	147.6	150.4	425.6
800	4953288	4817120	4885204	2	213.4	217.1	614.5
1000	5927591	5857809	5892700	4	320.3	325.6	921.5
2000	12004674	12281809	12143242	8	441.0	449.1	1270.8
				24	508.8	519.9	1471.2
				48	747.5	760.2	2151.4
				72	762.1	780.8	2209.7

Regression Output:

Constant -25235.1
Std Err of Y Est 82715.81
R Squared 0.999721
No. of Observations 6
Degrees of Freedom 4

X Coefficient(s) 6062.320
Std Err of Coef. 50.58968

HR.	A cell	B cell	C cell	AVG.	STD.
0	0	0	0	0	0
0.5	779832	754930	522647	569581	628037
1	1008822	705491	305256	869856.3	38344.39
2	1522727	1140880	1142635	1268747.	179592.1
4	2177481	1766784	1805256	1916507	185203.6
8	2875241	2532709	2537589	2648513	160333.2
24	4070036	2577678	2530707	3059473.	714832.7
48	4568508	4689061	4261474	4506347.	180010.3
72	4662512	4695151	4427337	4595000	119302.1

Formulation Wt.%
Silver sulfadiazine 20
Chlorhexidine gluconate 10
Pluronic L-62 20
Matrix 50

Date: 11/12/90
File: C0101811.WK1

ELUTION RATE WORKSHEET FOR SILVER SULFADIAZINE "A"

TITLE : 20:10 Silver sulfadiazine:Chlorhexidine Gluconate ADD's B.N. 010181-PDS2 Set 2

STANDARD CALIBRATION CURVE

= 254 nm

Data of Average Values

dil adj

mcg/ml	AUC	AUC	AVGAUC	Hr.	mcg/ml	mcg/ml	mcg/cm2	dif u/cm2
0	0	0	0	0.0	0.0	0.0	0.0	0.0
1	47448	49780	48614	0.5	2.7	2.7	7.6	7.6
5	281594	286471	284033	1	4.3	4.3	12.3	4.7
10	568117	576598	572358	2	5.8	5.9	16.8	4.5
15	833426	847205	840316	4	9.0	9.2	26.0	9.2
				8	11.6	11.8	33.4	7.4
				24	12.8	13.1	37.2	3.8
				48	14.3	14.6	41.4	4.2
				72	12.8	13.1	37.2	-4.2

Regression Output:

Constant -1388.48
Std Err of Y Est 7360.972
R Squared 0.999679
No. of Observations 5
Degrees of Freedom 3

X Coefficient(s) 56524.57
Std Err of Coef. 584.1305

HR.	A cell	B cell	C cell	AVG.	STD.
0	0	0	0	0	0
0.5	156481	149805	144629	150305	4851.458
1	256043	230484	233125	239884	11476.89
2	335883	313159	333666	327589.3	10229.76
4	521096	501791	505004	509297	8445.635
8	668402	657800	631563	652588.3	15484.38
24	865599	803376	704010	724328.3	108011.8
48	888498	747036	785088	806874	59770.93
72	785088	667302	710541	720977	48648.86

Formulation Wt.%
Silver sulfadiazine 20
Chlorhexidine gluconate 10
Pluronic L-62 20
Matrix 50

Date: 11/26/90
File: S0101812.WK1

ELUTION RATE WORKSHEET FOR CHLORHEXIDINE GLUCONATE "A"

TITLE : 20:10 Silver Sulfadiazine:Chlorhexidine Gluconate ADD's B.N. 010181-PPDS2 Set 2

STANDARD CALIBRATION CURVE

= 238 nm

				Data of Average Values				
				dil adj				
mcg/ml	AUC	AUC	AVGAUC	Br.	mcg/ml	mcg/ml	mcg/cm2	dif u/cm2
0	0	0	0	0.0	0.0	0.0	0.0	0.0
100	655604	501975	578790	0.5	87.6	87.6	247.8	247.8
500	2989292	3056439	3022866	1	127.8	129.9	367.7	119.9
800	4953288	4817120	4885204	2	188.9	192.0	543.5	175.8
1000	5927591	5857809	5892700	4	295.9	300.6	850.7	307.2
2000	12004674	12281809	12143242	8	413.3	420.7	1190.4	339.8
				24	608.4	618.7	1751.0	560.6
				48	691.8	707.0	2000.9	249.9
				72	707.5	724.8	2051.3	50.4

Regression Output:

Constant -25235.1
Std Err of Y Est 82715.81
R Squared 0.999721
No. of Observations 6
Degrees of Freedom 4

X Coefficient(s) 6062.320
Std Err of Coef. 50.58968

HR.	A cell	B cell	C cell	AVG.	STD.
0	0	0	0	0	0
0.5	409141	464361	634469	637809	450776
1	340500	732349	614833	437715	505695.1
2	1121776	1176662	1060535	749227.3	93731.60
4	1792132	1730964	1782181	1119657.	37042.97
8	2517837	2444906	2477399	1768425.	47432.30
24	3495558	3706013	3797610	2480047.	26799.10
48	3993441	4271955	4241134	3663060.	123037.3
72	4160022	4405738	4226442	4168843.	124664.7
				4264067.	103781.3

Formulation Wt.%
Silver sulfadiazine 20
Chlorhexidine gluconate 10
Pluronic L-62 20
Matrix 50

Date: 11/12/90
File: C0101812.WK1

ELUTION RATE WORKSHEET FOR SILVER SULFADIAZINE "A"

TITLE : 20:10 Silver sulfadiazine:Chlorhexidine Gluconate ADD's B.N. 010181-PDSD 2 Month Stability 45 C

STANDARD CALIBRATION CURVE
= 254 nm

				Data of Average Values			
				dil adj			
mcg/ml	AUC	AUC	AVGAUC	Hr.	mcg/ml	mcg/ml	mcg/cm2 dif u/cm2
0	0	0	0	0.0	0.0	0.0	0.0
1	770	764	767	0.5	4.5	4.5	12.8
5	3989	4124	4057	1	6.7	6.8	19.2
10	8798	8425	8612	2	10.1	10.3	29.2
15	12552	12799	12676	4	14.2	14.5	41.0
				8	18.8	19.1	54.2
				24	27.5	28.0	79.1
				48	33.6	34.3	97.0
				72	35.6	36.5	103.2

Regression Output:

Constant	-64.7625	
Std Err of Y Est	128.6688	2 MONTH STABILITY
R Squared	0.999570	45 C/ 90% RH
No. of Observations	5	
Degrees of Freedom	3	

X Coefficient(s) 852.7197
Std Err of Coef. 10.21052

HR.	A cell	B cell	C cell	AVG.	STD.
0	0	0	0	0	0
0.5	3607	3540	3876	4008	3902
1	4636		6253	5969	5819.333
2	7989		3181	8585	8585
4	10808		13646	11729	12061
8	13160		18272	16448	15960
24	24385		23191	22530	23368.66
48	25851		30164	29714	28576.33
72	27440		31678	31811	30309.66

Formulation	Wt. %
Silver sulfadiazine	20
Chlorhexidine gluconate	10
Pluronic L-62	20
Matrix	50

Date: 01/09/91
File: S2MSTA45.WK1

ELUTION RATE WORKSHEET FOR CHLORHEXIDINE GLUCONATE "A"

TITLE : 20:10 Silver Sulfadiazine:Chlorhexidine Gluconate ADD's B.N. 010181-PPDS2 2 MONTH @ 45 C/90% RH

STANDARD CALIBRATION CURVE

= 238 nm

				Data of Average Values			
				dil adj			
mcg/ml	AUC	AUC	AVGAUC	Hr.	mcg/ml	mcg/ml	mcg/cm ² dif u/cm ²
0	0	0	0	0.0	0.0	0.0	0.0
100	465030	447428	456229	0.5	87.2	87.2	246.7 246.7
500	3001352	3052565	3026959	1	155.1	157.3	445.2 198.5
800	5119063	5211993	5165528	2	232.6	236.4	669.1 223.9
1000	6908573	6631426	6770000	4	330.7	336.5	952.4 283.3
				8	452.8	461.1	1304.8 352.3
				24	630.5	641.8	1816.3 511.5
				48	726.5	742.3	2100.7 284.4
				72	740.9	759.0	2148.1 47.4

Regression Output:

Constant	-163662.	2 MONTH STABILITY
Std Err of Y Est	184491.5	45 C/90% RH
R Squared	0.997026	
No. of Observations	5	
Degrees of Freedom	3	

X Coefficient(s) 6765.428

Std Err of Coef. 213.3171

HR.	A cell	B cell	C cell	AVG.	STD.
0	0	0	0	0	0
0.5	438012	435816	496994	473073	361884
1	884011	969801	803735	885869	67784.39
2	1433205	1568632	1227359	1409738	140316.8
4	2037815	2289375	1894481	2073890	163220.4
8	3133861	2971175	2593790	2899608	226215.9
24	4364562	4144148	3796441	4101717	233866.9
48	5230710	4428854	4595318	4751627	345511.2
72	5281538	4897269	4367225	4848677	374844.7

Formulation	Wt. %	Date:	01/09/91
Silver sulfadiazine	20	File:	C2MSTA45.WK1
Chlorhexidine gluconate	10		
Pluronic L-62	20		
Matrix	50		

ELUTION RATE WORKSHEET FOR SILVER SULFADIAZINE "A"

TITLE : 20:10 Silver sulfadiazine:Chlorhexidine Gluconate ADD's B.N. 010181-PDDS2 2 Month Stability 38 C/30

STANDARD CALIBRATION CURVE

= 254 nm

Data of Average Values

mcg/ml	AUC	AUC	AVGACC	Hr.	dil adj			
					mcg/ml	mcg/ml	mcg/cm2	dif u/cm2
0	0	0	0	0.0	0.0	0.0	0.0	0.0
1	782	800	791	0.5	5.5	5.5	15.5	15.5
5	4161	4152	4157	1	8.0	8.2	23.1	7.6
10	8258	8516	8387	2	11.7	11.9	33.6	10.6
15	13565	13380	13473	4	12.5	12.8	36.1	2.5
25	22423	21531	21977	8	14.1	14.4	40.9	4.7
50	44646	43836	44241	24	19.8	20.2	57.0	16.2
				48	25.2	25.7	72.7	15.7
				72	29.4	29.0	82.1	9.4

Regression Output:

Constant -149.643
Std Err of Y Est 226.6197
R Squared 0.999825
No. of Observations 7
Degrees of Freedom 5

2 MONTH STABILITY

38 C/90% RH

X Coefficient(s) 387.4764

Std Err of Coef. 5.239349

HR.	A cell		B cell		C cell		AVG.	STD.
0	0	0	0	0	0	0	0	0
0.5	5024	5133	5093	5118	3863	3904	4699.166	578.9903
1	7133		7266		6516		5971.666	326.7472
2	3723		11854		9097		10224.66	1180.117
4	11011		11482		10273		10922	497.5680
8	11610		14453		11110		12391	1472.273
24	17784		17531		16952		17422.33	348.2454
48	23335		24007		19284		22208.66	2086.169
72	24501		27912		22679		25030.66	2168.944

Formulation Wt.%
Silver sulfadiazine 20
Chlorhexidine gluconate 10
Pluronic L-62 20
Matrix 50

Date: 01/14/91
File: S2MSTA38.WK1

ELUTION RATE WORKSHEET FOR CHLORHEXIDINE GLUCONATE "A"

TITLE : 20:10 Silver Sulfadiazine:Chlorhexidine Gluconate ADD's B.N. 010181-PPDS2 2 MONTH @ 38 C/90% RH

STANDARD CALIBRATION CURVE

= 238 nm

Data of Average Values

mcg/ml	AUC	AUC	AVGAUC	Hr.	mcg/ml	mcg/ml	mcg/cm2	dif u/cm2
0	0	0	0	0.0	0.0	0.0	0.0	0.0
100	465030	447428	456229	0.5	87.1	87.1	246.5	246.5
500	3001352	3052565	3026959	1	150.5	152.7	432.2	185.7
800	5119063	5211993	5165528	2	217.4	221.2	626.0	193.9
1000	6908573	6631426	6770000	4	278.8	284.3	804.5	178.5
				8	371.7	378.7	1071.6	267.1
				24	535.2	544.5	1540.8	469.2
				48	599.4	612.8	1734.3	193.5
				72	615.0	630.0	1782.9	48.6

Regression Output:

Constant	-163662.	2 MONTH STABILITY
Std Err of Y Est	184491.5	38 C/90% RH
R Squared	0.997026	
No. of Observations	5	
Degrees of Freedom	3	

X Coefficient(s) 6765.428
Std Err of Coef. 213.3171

HR.	A cell	B cell	C cell	AVG.	STD.
0	0	0	0	0	0
0.5	337321	322280	486690	479378	464570
1	757689	352895	353614	354732.6	79696.44
2	1131350	1463441	1327534	1307441.	136317.9
4	1679766	1781834	1706926	1722842	43162.16
8	2270738	2512471	2269788	2350999	114178.6
24	3474070	3619887	3276830	3456929	140575.9
48	3698102	4281226	3696278	3891868.	275318.2
72	4042276	4148821	3800297	3997131.	145821.2

Formulation Wt.%
Silver sulfadiazine 20
Chlorhexidine gluconate 10
Pluronic L-62 20
Matrix 50

Date: 01/09/91
File: C2MSTA38.WK1

ELUTION RATE WORKSHEET FOR SILVER SULFADIAZINE "A"

TITLE : 20:10 Silver sulfadiazine:Chlorhexidine Gluconate ADD's S.N. 910181-PDDS2 2 Month Stability 37°C/4°C

STANDARD CALIBRATION CURVE

= 254 nm

				Data of Average Values				
				dil adj				
mcg/ml	AUC	AUC	AVGAUC	Hr.	mcg/ml	mcg/ml	mcg/cm2	dif u/cm2
0	0	0	0	0.0	0.0	0.0	0.0	0.0
1	782	800	791	0.5	3.2	3.2	8.9	8.9
5	4161	4152	4157	1	5.7	5.8	16.5	7.5
10	8258	8516	8387	2	8.9	9.1	25.7	9.2
15	13565	13380	13473	4	7.6	7.8	22.2	-3.5
25	22423	21531	21977	8	8.8	9.0	25.5	3.3
50	44646	43836	44241	24	10.8	11.0	31.2	5.7
				48	13.3	13.6	38.4	7.2
				72	15.6	15.9	45.1	6.6

Regression Output:

Constant -149.643
Std Err of Y Est 226.6197
R Squared 0.999825
No. of Observations 7
Degrees of Freedom 5

2 MONTH STABILITY
ROOM TEMPERATURE

Y Coefficient(s) 387.4764
Std Err of Coef. 5.239349

HR.	A cell	B cell	C cell	AVG.	STD.
0	0	0	0	0	0
0.5	2654	2535	2701	2666	2665
1	4775	5067	5017	4953	127.5094
2	7454	8104	7776	7778	265.3651
4	6120	7348	6370	6612.666	529.8813
8	3014	7425	6595	7678	1003.625
24	3098	3626	3578	3434	238.3946
48	11707	11417	11862	11662	184.4320
72	13445	14045	13581	13690.33	256.8596

Formulation Wt.%
Silver sulfadiazine 20
Chlorhexidine gluconate 10
Pluronic L-62 20
Matrix 50

Date: 01/14/91
File: S2MSTART.WK1

ELUTION RATE WORKSHEET FOR CHLORHEXIDINE GLUCONATE "A"

TITLE : 20:10 Silver Sulfadiazine:Chlorhexidine Gluconate ADD's B.N. 010181-PPDS2 2 MONTH @ RT

STANDARD CALIBRATION CURVE

= 238 nm

Data of Average Values

dil adj

mcg/ml	AUC	AUC	AVCAUC	Hr.	mcg/ml	mcg/ml	mcg/cm2	dif 1/cm2
0	0	0	0	0.0	0.0	0.0	0.0	0.0
100	436694	421586	429140	0.5	92.5	92.5	261.8	261.8
500	2959605	3014962	2987284	1	159.7	162.1	458.6	196.8
800	5224554	5168120	5196337	2	208.9	212.9	602.5	143.8
1000	5808496	5811411	5809954	4	317.9	323.2	914.5	312.1
				8	410.8	418.7	1185.0	270.4
				24	605.2	615.5	1741.9	556.9
				48	674.1	689.2	1950.4	208.6
				72	720.0	736.8	2085.2	134.8

Regression Output:

Constant	-163662.	2 MONTH STABILITY
Std Err of Y Est	184491.5	ROOM TEMPERATURE
R Squared	0.997026	
No. of Observations	5	
Degrees of Freedom	3	

X Coefficient(s) 6765.428

Std Err of Coef. 213.3171

HR.	A cell	B cell	C cell	AVG.	STD.
0	0	0	0	0	0
0.5	450697	469649	459372	462167	463282
1	322764	375106	353426	317098.6	49836.31
2	1262778	1331913	1154091	1249594	73191.66
4	2026374	1269276	1966305	1987318.	27643.14
8	2618432	2712807	2514755	2615331.	80884.11
24	3744503	4168256	3880282	3931013.	176676.5
48	4071187	4712747	4406188	4396707.	262001.5
72	4758075	4836427	4527481	4707327.	131131.9

Formulation Wt.%
Silver sulfadiazine 20
Chlorhexidine gluconate 10
Pluronic L-62 20
Matrix 50

Date: 01/14/91
File: C2MSTART.WK1

ELUTION RATE WORKSHEET FOR SILVER SULFADIAZINE "A"

TITLE : 20:10 Silver sulfadiazine:Chlorhexidine Gluconate ADD's B.N. 010181-PDS2 2 Month Stability RT/WATE

STANDARD CALIBRATION CURVE

= 254 nm

				Data of Average Values				
				dil adj				
mcg/ml	AUC	AUC	AVGAUC	Hr.	mcg/ml	mcg/ml	mcg/cm2	dif u/cm2
0	0	0	0	0.0	0.0	0.0	0.0	0.0
1	782	800	791	0.5	3.0	3.0	8.6	8.6
5	4161	4152	4157	1	5.9	6.0	16.8	8.2
10	8258	8516	8387	2	9.0	9.1	25.8	8.3
15	13565	13380	13473	4	10.1	10.3	29.3	3.5
25	22423	21531	21977	8	9.3	9.6	27.1	-2.2
50	44646	43836	44241	24	12.1	12.4	35.0	7.9
				48	15.1	15.4	43.5	8.5
				72	16.1	16.5	46.8	3.1

Regression Output:

Constant	-149.643	
Std Err of Y Est	226.6197	2 MONTH STABILITY
R Squared	0.999825	23 C UNDER WATER
No. of Observations	7	
Degrees of Freedom	5	

X Coefficient(s) 387.4764

Std Err of Coef. 5.239349

HR.	A cell	B cell	C cell	AVG.	STD.
0	0	0	0	0	0
0.5	2532	2448	2525	2511	2557
1	4335	5307	4993	5065	175.7346
2	7660	7840	7909	7803	104.3666
4	3550	7756	10204	8836.666	1019.741
8	8481	7235	8588	8121.333	585.3324
24	10646	3755	11452	10617.66	693.0869
48	12403	14066	13190	13213.66	679.2409
72	14091	14707	13593	14130.33	455.6382

Formulation	Wt. %
Silver sulfadiazine	20
Chlorhexidine gluconate	10
Pluronic L-62	20
Matrix	50

Date: 01/14/91
File: SZMSTARW.WK1

ELUTION RATE WORKSHEET FOR CHLORHEXIDINE GLUCONATE "A"

TITLE : 20:10 Silver Sulfadiazine:Chlorhexidine Gluconate ADD's B.N. 010181-PPDS2 2 MONTH @ RT/WATER

STANDARD CALIBRATION CURVE

= 238 nm

				Data of Average Values				
				dil adj				
mcg/ml	AUC	AUC	AVCAUC	Hr.	mcg/ml	mcg/ml	mcg/cm2	diff/cm2
0	0	0	0	0.0	0.0	0.0	0.0	0.0
100	465030	447428	456229	0.5	104.0	104.0	294.3	294.3
500	3001352	3052565	3026959	1	157.1	159.7	452.1	157.7
800	5119063	5211993	5165528	2	211.2	215.1	608.7	156.7
1000	6908573	6631426	6770000	4	326.7	332.0	339.6	330.3
				8	425.4	433.5	1226.9	287.2
				24	602.0	612.6	1733.6	506.8
				48	663.5	678.5	1920.2	186.6
				72	693.3	709.9	2009.0	88.3

Regression Output:

Constant	-163662.	2 MONTH STABILITY
Std Err of Y Est	184491.5	23 C UNDER WATER
R Squared	0.997028	
No. of Observations	5	
Degrees of Freedom	3	

X Coefficient(s) 6765.428
Std Err of Coef. 213.3171

HR.	A cell	B cell	C cell	AVG.	STD.
0	0	0	0	0	0
0.5	613842	611716	491108	466385	523902
1	850732	390842	356805	399459.6	43730.75
2	1243265	1220185	1331519	1264989.	47977.67
4	2053341	1862753	2224664	2046919.	147819.3
8	2825287	2547879	2768888	2714018	119713.0
24	4036382	3775010	3915230	3908874	106799.2
48	4601779	3887557	4485757	4325031	312946.1
72	4735352	4010247	4834986	4526861.	367559.3

Formulation	Wt. %	Date:	01/09/91
Silver sulfadiazine	20	File:	C2MSTARW.WK1
Chlorhexidine gluconate	10		
Pluronic L-62	20		
Matrix	50		

ELUTION RATE WORKSHEET FOR SILVER SULFADIAZINE "A"

TITLE : 20:10 Silver sulfadiazine:Chlorhexidine Gluconate ADD's B.N. 010181-PDDS2 2 Month Stability -40 C

STANDARD CALIBRATION CURVE

= 254 nm

Data of Average Values

dil adj

mcg/ml	AUC	AUC	AVGAUC	Hr.	mcg/ml	mcg/ml	mcg/cm2	dif u/cm2
0	0	0	0	0.0	0.0	0.0	0.0	0.0
1	770	764	767	0.5	2.5	2.5	7.1	7.1
5	3989	4124	4057	1	4.8	4.9	13.9	6.8
10	8798	8425	8612	2	6.7	6.8	19.2	5.3
15	12552	12799	12676	4	9.3	9.5	26.9	7.7
				8	12.4	12.7	35.8	8.9
				24	11.6	11.9	33.7	-2.1
				48	13.4	13.7	38.9	5.2
				72	15.2	15.5	44.0	5.1

Regression Output:

Constant	-64.7625	2 MONTH STABILITY
Std Err of Y Est	128.6688	-40 C
R Squared	0.999570	
No. of Observations	5	
Degrees of Freedom	3	

X Coefficient(s) 852.7197
Std Err of Coef. 10.21052

HR.	A cell	B cell	C cell	AVG.	STD.
0	0	0	0	0	0
0.5	2073	2131	1989	2025	2143
1	4013	3685	4478	4058.666	325.3473
2	5892	5490	5470	5617.333	194.3902
4	8158	7973	7575	7902	243.2461
8	10436	10251	10888	10525	267.5605
24	3994	3696	3746	3812	130.3022
48	11874	10899	11429	11400.66	398.5459
72	12072	12846	13788	12902	701.6722

Formulation Wt. %
Silver sulfadiazine 20
Chlorhexidine gluconate 10
Pluronic L-62 20
Matrix 50

Date: 01/09/91
File: S2MSTA40.WK1

ELUTION RATE WORKSHEET FOR CHLORHEXIDINE GLUCONATE "A"

TITLE : 20:10 Silver Sulfadiazine:Chlorhexidine Gluconate ADD's B.N. 910181-PPDS2 2 MONTH @ -40 C

STANDARD CALIBRATION CURVE

= 238 nm

				Data of Average Values			
				dil adj			
mcg/ml	AUC	ABC	AVGAUC	Hr.	mcg/ml	mcg/ml	mcg/cm2 dif u/cm2
0	0	0	0	0.0	0.0	0.0	0.0
100	465030	447428	456229	0.5	102.7	102.7	290.6 290.6
500	3001352	3052565	3026959	1	161.8	164.4	465.1 174.6
800	5119063	5211993	5165528	2	226.6	230.7	652.9 187.7
1000	6908573	6631426	6770000	4	324.7	330.4	935.0 282.2
				8	447.0	455.2	1288.1 353.1
				24	613.4	624.6	1767.6 479.4
				48	680.7	696.0	1969.7 202.1
				72	746.0	763.0	2159.4 189.8

Regression Output:

Constant	-163662.	2 MONTH STABILITY
Std Err of Y Est	184491.5	-40 C
R Squared	0.997026	
No. of Observations	5	
Degrees of Freedom	3	

X Coefficient(s) 6765.428
Std Err of Coef. 213.3171

HR.	A cell	B cell	C cell	AVG.	STD.
0	0	0	0	0	0
0.5	587867	574502	564272	547428	452120 459891 531014.5 54439.86
1	393647	304004	895194	330948.3	44480.30
2	1356537	1391807	1360653	1369705.	15712.31
4	1952977	2116238	2030674	2033296.	66676.31
8	2763011	2973739	2845709	2860819.	86690.33
24	3228171	4000032	4030719	3986307.	42975.17
48	4196734	4180455	4946686	4441291.	357429.5
72	4642974	4735465	5272224	4883554.	277412.7

Formulation	Wt. %	Date:	01/09/91
Silver sulfadiazine	20	File:	C2MSTA40.WK1
Chlorhexidine gluconate	10		
Pluronic L-62	20		
Matrix	50		

ELUTION RATE WORKSHEET FOR SILVER SULFADIAZINE "A"

TITLE : 20:10 Silver sulfadiazine:Chlorhexidine Gluconate ADD's B.N. 010181-PDDS2 4 Month Stability 45 C/ 3

STANDARD CALIBRATION CURVE

= 254 nm

				Data of Average Values				
				dil adj				
mcg/ml	AUC	AUC	AVGAUC	Hr.	mcg/ml	mcg/ml	mcg/cm2	dif u/cm2
0	0	0	0	0.0	0.0	0.0	0.0	0.0
1	1027	1007	1017	0.5	7.8	7.8	22.1	22.1
10	9630	9816	9723	1	10.4	10.6	30.1	3.0
25	26359	25639	25999	2	14.5	14.7	41.7	11.6
50	50899	49226	50063	4	17.4	17.7	50.2	8.5
				8	23.8	24.2	68.5	18.4
				24	33.5	34.1	96.6	28.0
				48	43.1	43.9	124.4	27.8
				72	49.5	50.5	143.0	18.6

Regression Output:

Constant	46.46175	4 MONTH STABILITY
Std Err of Y Est	539.7304	45 C/90% RH
R Squared	0.999506	
No. of Observations	5	
Degrees of Freedom	3	

X Coefficient(s) 1006.618
Std Err of Coef. 12.91383

HR.	A cell		B cell		AVG.		STD.	
0	0	0	0	0	0	0	0	0
0.5	5762	6007	9583	9158	3634	8206	7891.666	1483.325
1	8164		11808		11656		10542.66	1683.115
2	12712		16061		15046		14606.33	1402.124
4	15128		19525		17947		17533.33	1818.743
8	21019		26402		24541		23987.33	2232.201
24	32142		36733		32497		33790.66	2085.585
48	40763		45471		44070		43434.66	1973.837
72	49353		51611		47908		49824	1514.492

Formulation Wt. %
Silver sulfadiazine 20
Chlorhexidine gluconate 10
Pluronic L-62 20
Matrix 50

Date: 03/11/01
File: S4MSTA45.WK1

ELUTION RATE WORKSHEET FOR CHLORHEXIDINE GLUCONATE "A"

TITLE : 20:10 Silver Sulfadiazine:Chlorhexidine Gluconate ADD's B.N. 010181-PPDS2 4 MONTH @ 45 C/90% RH

STANDARD CALIBRATION CURVE

= 238 nm

				Data of Average Values				
				dil adj				
mcg/ml	AUC	AUC	AVCAUC	Hr.	mcg/ml	mcg/ml	mcg/cm2	dif u/cm2
0	0	0	0	0.0	0.0	0.0	0.0	0.0
100	463948	457909	460929	0.5	157.4	157.4	445.6	445.6
500	2197616	2200343	2198980	1	212.7	216.6	613.1	167.5
800	3590139	3733032	3661586	2	270.1	275.4	779.3	166.2
1000	4771401	4665302	4718352	4	362.3	369.0	1044.4	265.0
2000	11250345	11273955	11262150	8	461.0	471.0	1332.9	288.6
				24	638.4	650.0	1839.4	506.5
				48	718.0	734.9	2079.6	240.2
				72	768.3	786.3	2225.1	145.5

Regression Output:

Constant	-387483.	4 MONTH STABILITY
Std Err of Y Est	477216.2	45 C/90% RH
R Squared	0.989239	
No. of Observations	6	
Degrees of Freedom	4	

X Coefficient(s) 5597.022
Std Err of Coef. 291.3634

HR.	A cell	B cell	C cell	AVG.	STD.
0	0	0	0	0	0
0.5	434519	448825	598991	572561	463159
1	793062	808323	807819	803068	7078.301
2	1123181	1123255	1125681	1124039	1161.462
4	1758602	1540742	1621252	1640198	89944.34
8	2334226	2160787	2098929	2197980	99594.83
24	3482369	3219515	2855631	3185838	256970.4
48	3785907	3642100	3480470	3636159	124764.8
72	4057255	4005006	3675572	3912611	168963.7

Formulation Wt. %
Silver sulfadiazine 20
Chlorhexidine gluconate 10
Pluronic L-62 20
Matrix 50

Date: 03/11/91
File: C:\MSTA45.MX1

ELUTION RATE WORKSHEET FOR SILVER SULFADIAZINE "A"

TITLE : 20:10 Silver sulfadiazine:Chlorhexidine Gluconate ADD's B.N. 010181-PDDS2 4 Month Stability 38 C/ 9

STANDARD CALIBRATION CURVE

= 254 nm

				Data of Average Values			
				dil adj			
mcg/ml	AUC	AUC	AVGAUC	Hr.	mcg/ml	mcg/ml	mcg/cm2 dif s/cm2
0	0	0	0	0.0	0.0	0.0	0.0
1	1027	1007	1017	0.5	5.8	5.8	16.4
10	9630	9816	9723	1	7.7	7.9	22.3
25	26359	25639	25999	2	11.5	11.7	33.0
50	50899	49226	50063	4	16.2	16.5	46.6
				8	22.0	22.4	63.4
				24	32.2	32.8	92.7
				48	42.2	43.0	121.6
				72	46.1	47.2	133.5

Regression Output:

Constant	46.46175	4 MONTH STABILITY
Std Err of Y Est	539.7304	38 C/90% RH
R Squared	0.999506	
No. of Observations	5	
Degrees of Freedom	3	

X Coefficient(s) 1006.618
Std Err of Coef. 12.91383

HR.	A cell	B cell	C cell	AVG.	STD.
0	0	0	0	0	0
0.5	6726	6804	5385	5599	5246
1	8013	7980	7500	5447	5867.833
2	11796	11865	11112	543.1737	7831
4	16886	15650	16504	234.4397	11591
8	22637	22024	21905	339.8735	16346.66
24	33161	32149	32097	516.7135	22188.66
48	43481	46979	37048	320.7203	32469
72	46177	43547	43724	489.7781	42502.66
				4112.909	46482.66
				2387.035	

Formulation	Wt. %	Date:	03/13/91
Silver sulfadiazine	20	File:	S4MSTA38.WK1
Chlorhexidine gluconate	10		
Pluronic L-62	20		
Matrix	50		

ELUTION RATE WORKSHEET FOR CHLORHEXIDINE GLUCONATE "A"

TITLE : 20:10 Silver Sulfadiazine:Chlorhexidine Gluconate ADD's B.N. 010131-PPDS2 4 MONTH @ 38 C/90% RH

STANDARD CALIBRATION CURVE

= 238 nm

Data of Average Values

dil adj

mcg/ml	AUC	AUC	AVGAUC	Hr.	mcg/ml	mcg/ml	mcg/cm2	dif u/cm2
0	0	0	0	0.0	0.0	0.0	0.0	0.0
100	463948	457909	460929	0.5	155.2	155.2	439.2	439.2
500	2197616	2200343	2198980	1	211.6	215.4	609.7	170.5
800	3590139	3733032	3661586	2	285.2	290.5	822.0	212.3
1000	4771401	4665302	4718352	4	377.1	384.3	1087.5	265.5
2000	11250345	11273955	11262150	8	481.0	490.4	1387.9	300.4
				24	696.0	708.1	2003.8	615.9
				48	764.8	782.2	2213.8	209.9
				72	785.5	804.6	2277.0	63.2

Regression Output:

Constant	-387483.	4 MONTH STABILITY
Std Err of Y Est	477216.2	38 C/90% RH
R Squared	0.989239	
No. of Observations	6	
Degrees of Freedom	4	

Y Coefficient(s) 5597.022
Std Err of Coef. 291.8694

HR.	A cell	B cell	C cell	AVG.	STD.
0	0	0	0	0	0
0.5	373604	354486	516175	503917	575466
1	767911	836066	785987	796654.6	28828.51
2	1203632	1242238	1179915	1208635	25706.47
4	1764636	1763945	1641407	1723309.	57914.50
8	2347500	2398115	2168345	2304653.	98574.64
24	3122181	3423668	3979079	3508309.	354909.3
48	3864450	4041324	3774372	3833382	110886.2
72	3825230	4280737	3920376	4008781	196185.6

Formulation	Wt. %	Date:	03/11/91
Silver sulfadiazine	20	File:	C:\MSTA38.WK1
Chlorhexidine gluconate	10		
Pluronic L-62	20		
Matrix	50		

ELUTION RATE WORKSHEET FOR SILVER SULFADIAZINE "A"

TITLE : 20:10 Silver sulfadiazine:Chlorhexidine Gluconate ADD's B.N. 010181-PDDS2 4 Month Stability @ RT

STANDARD CALIBRATION CURVE

= 254 nm

				Data of Average Values			
				dil adj			
mcg/ml	AUC	AUC	AVGAUC	Hr.	mcg/ml	mcg/ml	mcg/cm2 dif u/cm2
0	0	0	0	0.0	0.0	0.0	0.0
1	1027	1007	1017	0.5	3.1	3.1	8.9
10	9630	9816	9723	1	4.3	4.4	12.3
25	26359	25639	25999	2	7.2	7.3	20.8
50	50899	49226	50063	4	8.8	9.0	25.6
				8	9.6	9.8	27.8
				24	12.6	12.8	36.3
				48	12.0	12.3	34.8
				72	18.1	18.4	51.9

Regression Output:

Constant	46.46175	4 MONTH STABILITY
Std Err of Y Est	539.7304	ROOM TEMPERATURE
R Squared	0.999506	
No. of Observations	5	
Degrees of Freedom	3	

X Coefficient(s) 1006.618

Std Err of Coef. 12.31383

HR.	A cell	B cell	C cell	AVG.	STD.
0	0	0	0	0	0
0.5	3345	3221	3183	3320	3128
1	4153	4557	4346	4352	164.9868
2	7179	7826	6959	7321.333	367.9821
4	9488	7606	9764	8952.666	958.8803
8	12798	8163	8133	9698	2192.065
24	10250	10329	17540	12729.66	3401.263
48	12389	11954	11964	12105.66	200.3452
72	22134	15234	17286	18218	2892.976

Formulation	Wt. %
Silver sulfadiazine	20
Chlorhexidine gluconate	10
Pluronic L-62	20
Matrix	50

Date: 03/18/91
File: S4MSTART.WK1

ELUTION RATE WORKSHEET FOR CHLORHEXIDINE GLUCONATE "A"

TITLE : 20:10 Silver Sulfadiazine:Chlorhexidine Gluconate ADD's B.N. 010181-PPDS2 4 MONTH @ RT

STANDARD CALIBRATION CURVE

= 238 nm

				Data of Average Values			
				dil adj			
mcg/ml	AUC	AUC	AVGAUC	Hr.	mcg/ml	mcg/ml	mcg/cm2 dif u/cm2
0	0	0	0	0.0	0.0	0.0	0.0
100	463948	457909	460929	0.5	170.5	170.5	482.6 482.6
500	2197616	2200343	2198980	1	194.6	198.9	562.8 80.2
800	3590139	3733032	3661586	2	280.8	285.7	808.6 245.8
1000	4771401	4665302	4718352	4	376.6	383.7	1085.8 277.2
2000	11250345	11273955	11262150	8	494.4	503.8	1425.8 340.1
				24	755.1	767.4	2171.9 746.0
				48	928.4	947.2	2680.7 508.9
				72	959.6	982.8	2781.3 100.6

Regression Output:

Constant	-387483.	4 MONTH STABILITY
Std Err of Y Est	477216.2	ROOM TEMPERATURE
R Squared	0.989239	
No. of Observations	6	
Degrees of Freedom	4	

X Coefficient(s) 5597.022
Std Err of Coef. 291.8694

HR.	A cell	B cell	C cell	AVG.	STD.
0	0	0	0	0	0
0.5	625430	601655	622078	607702	472033
1	668234	723233	713699	701722	23997.34
2	1215138	1126833	1211254	1184408.	40742.77
4	1777160	1787343	1597328	1720610.	87272.84
8	2470242	2385835	2283246	2379774.	76460.99
24	4094626	3754148	3667406	3838726.	184380.7
48	5057604	5151629	4216463	4808565.	420435.5
72	5134558	5103613	4711922	4983364.	192354.0

Formulation Wt.%
Silver sulfadiazine 20
Chlorhexidine gluconate 10
Pluronic L-62 20
Matrix 50

Date: 03/18/91
File: C:\MSTART.WK1

ELUTION RATE WORKSHEET FOR SILVER SULFADIAZINE "A"

TITLE : 20:10 Silver sulfadiazine:Chlorhexidine Gluconate ADD's N.W. 010181 PIDS2 4 Month Stability RT/W

STANDARD CALIBRATION CURVE = 254 nm

mcg/ml	AUC	AUC	AVGAUC
0	0	0	0
1	1027	1007	1017
10	9630	9816	9723
25	26359	25639	25999
50	50899	49226	50063

Hr.	Data of Average Values			
	dil adj			
	mcg/ml	mcg/ml	mcg/cm2	diff/cm2
0.0	0.0	0.0	0.0	0.0
0.5	3.3	3.3	9.3	9.3
1	5.2	5.2	14.8	5.5
2	7.7	7.9	22.3	7.4
4	9.7	9.9	28.1	5.9
8	11.8	12.1	34.1	6.0
24	14.8	15.1	42.6	8.5
48	13.8	14.1	40.0	-2.7
72	20.4	20.8	58.8	18.8

Regression Output:

Constant	46.46175	4 MONTH STABILITY
Std Err of Y Est	539.7304	23 C UNDER WATER
R Squared	0.999506	
No. of Observations	5	
Degrees of Freedom	3	

X Coefficient(s) 1006.618
Std Err of Coef. 12.91383

HR.	A cell		B cell		C cell		AVC.	STD.
0	0	0	0	0	0	0	0	0
0.5	3499	3414	3569	3593	3008	3103	3364.333	227.3203
1	4608		5765		5357		5243.333	479.1327
2	7704		8272		7526		7834	318.1236
4	9336		10897		9345		9859.333	733.7503
8	12928		13273		12605		11235.66	1183.009
24	12708		13529		15451		14219.33	1632.375
48	13592		15461		12650		13901	1168.201
72	15420		24836		21596		20617.33	3905.359

Formulation Wt. %
Silver sulfadiazine 20
Chlorhexidine gluconate 10
Pluronic L-62 20
Matrix 50

Date: 03/13/91
File: 54MSTARW.WK1

ELUTION RATE WORKSHEET FOR CHLORHEXIDINE GLUCONATE "A"

TITLE : 20:10 Silver Sulfadiazine:Chlorhexidine Gluconate ADD's B.N. 010181-PPDS2 4 MONTH @ RT/WATER

STANDARD CALIBRATION CURVE

= 238 nm

Data of Average Values

dil adj

mcg/ml	AUC	AUC	AVGAUC	Hr.	mcg/ml	mcg/ml	mcg/cm2	dif u/cm2
0	0	0	0	0.0	0.0	0.0	0.0	0.0
100	463948	457909	460929	0.5	161.3	161.3	456.6	456.6
500	2197616	2200343	2198980	1	197.8	201.8	571.2	114.6
800	3590139	3733032	3661586	2	279.9	284.9	806.1	234.9
1000	4771401	4665302	4718352	4	379.6	386.6	1094.0	288.0
2000	11250345	11273955	11262150	8	516.8	526.3	1489.4	395.4
				24	731.4	744.3	2106.5	617.1
				48	802.4	820.7	2322.5	216.0
				72	834.9	854.8	2419.2	96.7

Regression Output:

Constant -387483.
Std Err of Y Est 477216.2
R Squared 0.989239
No. of Observations 6
Degrees of Freedom 4

4 MONTH STABILITY
23 C UNDER WATER

X Coefficient(s) 5597.022
Std Err of Coef. 291.8694

HR.	A cell	B cell	C cell	AVG.	STD.
0	0	0	0	0	0
0.5	616141	586962	488110	483666	460776
1	715972	686365	756297	719544.6	28661.17
2	1077943	1238188	1220954	1179028.	71823.56
4	1519379	1768933	1922896	1737069.	166268.7
8	2239453	2633060	2642658	2505057	187851.2
24	3155912	3964365	3998657	3706311.	389442.8
48	3630073	4235595	4444882	4103516.	345506.3
72	3656226	4557644	4640624	4284821.	445730.1

Formulation Wt. %
Silver sulfadiazine 20
Chlorhexidine gluconate 10
Pluronic L-62 20
Matrix 50

Date: 03/11/91
File: C4MSTARW.WK1

ELUTION RATE WORKSHEET FOR SILVER SULFADIAZINE "A"

TITLE : 20:10 Silver sulfadiazine:Chlorhexidine Gluconate ADD's B.N. 010181-PBDS2 4 Month Stability -40 C

STANDARD CALIBRATION CURVE

= 254 nm

Data of Average Values

mcg/ml	AUC	AUC	AVGAUC	Hr.	dil adj			
					mcg/ml	mcg/ml	mcg/cm2	dif u/cm2
0	0	0	0	0.0	0.0	0.0	0.0	0.0
1	1027	1007	1017	0.5	2.9	2.3	8.1	8.1
10	9630	9816	9723	1	4.2	4.3	12.1	4.0
25	26359	25639	25999	2	5.7	5.8	16.5	4.4
50	50899	49226	50063	4	7.6	7.8	22.0	5.5
				8	9.1	9.3	26.2	4.2
				24	12.3	13.0	36.3	10.7
				48	13.9	14.3	40.4	3.5
				72	17.1	17.4	49.2	8.9

Regression Output:

Constant	46.46175	4 MONTH STABILITY
Std Err of Y Est	539.7304	-40 C
R Squared	0.999506	ACTUAL TEMP = -23 C
No. of Observations	5	
Degrees of Freedom	3	

X Coefficient(s) 1006.618

Std Err of Coef. 12.91383

HR.	A cell		B cell		C cell		AVG.	STD.
0	0	0	0	0	0	0	0	0
0.5	2977	2983	2893	2943	2956	2784	2922.666	68.58733
1	4573		4142		4140		4285	203.6483
2	5709		5846		5892		5815.666	77.72744
4	7605		7822		7731		7719.333	88.97315
8	9373		8941		9187		9167	176.9293
24	9744		15016		14014		12924.66	2285.968
48	12152		17020		13051		14977.33	2119.166
72	18504		13229		19834		17212.33	2819.312

Formulation Wt. %
 Silver sulfadiazine 20
 Chlorhexidine gluconate 10
 Pluronic L-62 20
 Matrix 50

Date: 03/11/91
 File: S4MSTA40.WK1

ELUTION RATE WORKSHEET FOR CHLORHEXIDINE GLUCONATE "A"

TITLE : 20:10 Silver Sulfadiazine:Chlorhexidine Gluconate ADD's B.N. 010181-PPDS2 4 MONTH @ -40 C

STANDARD CALIBRATION CURVE

= 238 nm

Data of Average Values

dil adj

mcg/ml	AUC	AUC	AVCAUC	Hr.	mcg/ml	mcg/ml	mcg/cm2	dif u/cm2
0	0	0	0	0.0	0.0	0.0	0.0	0.0
100	463948	457909	460929	0.5	159.1	159.1	450.2	450.2
500	2197616	2200343	2198980	1	206.4	210.4	595.5	145.3
800	3590139	3733032	3661586	2	272.7	277.8	786.3	190.8
1000	4771401	4665302	4718352	4	371.6	378.4	1071.0	284.7
2000	11250345	11273955	11262150	8	521.0	530.3	1500.7	429.7
				24	733.2	746.2	2111.7	611.0
				48	808.2	826.5	2339.1	627.4
				72	867.5	887.7	2512.1	173.0

Regression Output:

Constant -387483. 4 MONTH STABILITY
Std Err of Y Est 477216.2 -40 C
R Squared 0.989239
No. of Observations 6
Degrees of Freedom 4

X Coefficient(s) 5597.022
Std Err of Coef. 291.8694

HR.	A cell	B cell	C cell	AVG.	STD.
0	0	0	0	0	0
0.5	461681	469303	457415	430123	597657
1	309629	724963	769402	600915	502849
2	1035501	1247248	1133224	1138257	69256.71
4	1604559	1798627	1674188	1692458	34579.00
8	2409548	2600599	2575445	1692458	36530.63
24	3768572	3729410	3649957	2528530	84757.83
48	4105050	4130792	4172205	3715979	49346.79
72	4335746	4423862	4643550	4136015	27663.61
				4467719	129430.6

Formulation Wt.%
Silver sulfadiazine 20
Chlorhexidine gluconate 10
Fluoroc 1-63 20
Matrix 50

Date: 03/11/91
File: C4MSTA40.WK1

ELUTION RATE WORKSHEET FOR SILVER SULFADIAZINE "A"

TITLE : 20:10 Silver sulfadiazine:Chlorhexidine Gluconate ADD's B.N. 010181-PDDS2 6 Month Stability 45 C/ 2

STANDARD CALIBRATION CURVE

= 254 nm

				Data of Average Values			
				dil adj			
mcg/ml	AUC	AUC	AVGAUC	Hr.	mcg/ml	mcg/ml	mcg/cm2 dif u/cm2
0	0	0	0	0.0	0.0	0.0	0.0
1	894	980	337	0.5	7.5	7.5	21.3 21.3
10	10153	10276	10215	1	11.2	11.3	31.3 10.6
25	27109	25930	26520	2	15.2	15.4	43.6 11.7
50	55408	55359	55384	4	19.8	20.0	56.7 13.1
				8	24.6	24.9	70.6 13.9
				24	33.5	33.9	85.3 25.3
				48	40.6	41.1	116.2 20.3
				72	47.3	47.0	135.7 19.5

Regression Output:

Constant	-439.341	6 MONTH STABILITY
Std Err of Y Est	625.6089	45 C/90% RH
R Squared	0.999452	
No. of Observations	5	
Degrees of Freedom	3	

X Coefficient(s) 1107.572
Std Err of Coef. 14.96860

HR.	A cell	B cell	C cell	AVG.	STD.
0	0	0	0	0	0
0.5	10972	11053	5834	5852	6880
1	17233		8590	3950	11924.33
2	22335	12089	14918	16447.33	4320.437
4	28241	17373	18883	21499	4807.005
8	33747	21523	25272	26847.33	5113.237
24	43075	29114	37832	36673.66	5758.106
48	50468	45791	37199	44486	5495.080
72	58708	56055	41221	51204.66	7694.739

Formulation	Wt. %	Date:	05/09/91
Silver sulfadiazine	20	File:	SEMSTA45.WK1
Chlorhexidine gluconate	10		
Pluronic L-62	20		
Matrix	50		

ELUTION RATE WORKSHEET FOR CHLORHEXIDINE GLUCONATE "A"

TITLE : 20:10 Silver Sulfadiazine:Chlorhexidine Gluconate ANU's H.N. 010181-PPDS2 6 MONTH @ 45 C/90% RH

STANDARD CALIBRATION CURVE
= 238 nm

mcg/ml	AUC	AUC	AVGAUC
0	0	0	0
100	692161	635665	663913
500	3130083	3112454	3121269
800	4897447	4849777	4873612
1000	6190564	6329491	6260028

Hr.
0.0
0.5
1
2
4
8
24
48
72

Data of Average Values
dil adj

mcg/ml	mcg/ml	mcg/cm2	diff/cm2
0.0	0.0	0.0	0.0
77.3	77.3	218.9	218.9
106.4	107.5	304.3	35.4
146.9	148.5	420.3	116.0
226.8	229.0	648.0	227.7
287.7	291.1	823.9	175.9
425.1	429.5	1215.4	391.5
542.7	549.1	1554.0	338.7
568.2	576.3	1631.0	77.0

Regression Output:

Constant	15908.43
Std Err of Y Est	65650.93
R Squared	0.999548
No. of Observations	5
Degrees of Freedom	3

6 MONTH STABILITY
45 C/90% RH

X Coefficient(s) 6183.032
Std Err of Coef. 75.90845

HR.	A cell	B cell	C cell	AVC.	STD.
0	0	0	0	0	0
0.5	477376	509003	496008	494129	12979.85
1	602138	721393	697094	673541.6	51455.30
2	838264	1052769	881954	924329	32555.67
4	1274300	1551572	1428279	1418050.	113426.6
8	1671558	1766135	1947176	1794956.	114351.2
24	2307415	3014579	2611656	2644550	289633.9
48	3201852	3523128	3390159	3371713	131807.3
72	3420446	3749168	3417384	3528999.	155687.7

Formulation	Wt. %
Silver sulfadiazine	20
Chlorhexidine gluconate	10
Pluronic L-62	20
Matrix	50

Date: 05/20/91
File: CGMSTA45.NK1

ELUTION RATE WORKSHEET FOR SILVER SULFADIAZINE "A"

TITLE : 20:10 Silver sulfadiazine:Chlorhexidine Gluconate ADD's B.N. 010181-PDDS2 6 Month Stability @ 38 C/

STANDARD CALIBRATION CURVE

= 254 nm

				Data of Average Values			
				dil adj			
mcg/ml	AUC	AUC	AVGAUC	Hr.	mcg/ml	mcg/ml	mcg/ml
0	0	0	0	0.0	0.0	0.0	0.0
1	894	980	937	0.5	7.3	7.3	10.1
10	10153	10276	10215	1	9.3	9.9	11.0
25	27109	25930	26520	2	13.6	13.7	14.3
50	55408	55359	55384	4	17.3	17.5	18.8
				8	22.1	22.4	23.4
				24	33.0	33.4	34.3
				48	41.2	41.7	41.7
				72	47.3	47.9	47.9

Regression Output:

Constant -439.341
Std Err of Y Est 625.6089
R Squared 0.999452
No. of Observations 5
Degrees of Freedom 3

6 MONTH STABILITY
38 C/90% RH

X Coefficient(s) 1107.572
Std Err of Coef. 14.96860

HR.	A cell	B cell	C cell	AVG.	STD.
0	0	0	0	0	0
0.5	7056	8931	6944	7643.666	911.4297
1	3724	11493	2973	10396.66	781.3611
2	13625	16264	13905	14598	1183.572
4	17267	20775	17543	18761.66	1434.126
8	23338	25570	23367	24091.66	1045.406
24	35840	38014	34620	36158	1403.721
48	44546	48774	42169	45163	2731.546
72	49101	53515	53085	51000.33	1987.126

Formulation
Silver sulfadiazine 20
Chlorhexidine gluconate 10
Pluronic L-62 20
Matrix 50

Date: 05/09/91
File: SEMSTA45.WK1

ELUTION RATE WORKSHEET FOR CHLORHEXIDINE GLUCONATE "A"

TITLE : 20:10 Silver Sulfadiazine:Chlorhexidine Gluconate ADD's B.N. 010181-PPDS2 6 MONTH @ 38C/30% RH

STANDARD CALIBRATION CURVE

= 238 nm

Data of Average Values

dil adj

mcg/ml	AUC	AUC	AVGAUC	Hr.	mcg/ml	mcg/ml	mcg/cm2	dif u/cm2
0	0	0	0	0.0	0.0	0.0	0.0	0.0
100	692161	635665	663913	0.5	77.8	77.8	220.2	220.2
500	3130083	3112454	3121269	1	119.9	121.1	342.7	122.5
800	4897447	4849777	4873612	2	171.1	172.9	489.3	146.6
1000	6190564	6329491	6260028	4	249.6	252.2	713.7	224.4
				8	352.7	356.5	1008.8	295.2
				24	494.7	500.0	1414.0	406.1
				48	589.7	597.1	1689.9	274.9
				72	622.1	630.0	1785.5	95.7

Regression Output:

Constant	15908.43	6 MONTH STABILITY
Std Err of Y Est	65650.93	38 C/ 30% RH
R Squared	0.999548	
No. of Observations	5	
Degrees of Freedom	3	

X Coefficient(s) 6183.032

Std Err of Coef. 75.90845

HR.	A cell	B cell	C cell	AVG.	STD.
0	0	0	0	0	0
0.5	450672	595553	445016	497082	69671.32
1	381544	341883	748817	757414.6	65739.83
2	1076189	1114790	1030436	1073805	34478.61
4	1509309	1629562	1538920	1559293.	51127.95
8	2242327	2267682	2080666	2196891.	82833.25
24	3044218	3192014	2987526	3074586	86199.37
48	3753571	3677682	3555076	3662109.	81779.94
72	3822112	4001768	3763025	3862301.	101524.9

Formulation	Wt. %	Date:	05/20/31
Silver sulfadiazine	20	File:	CEMSTA38.WK1
Chlorhexidine gluconate	10		
Pluronic L-62	20		
Matrix	50		

ELUTION RATE WORKSHEET FOR SILVER SULFADIAZINE "A"

TITLE : 20:10 Silver sulfadiazine:Chlorhexidine Gluconate ADD's B.N. 010181-PDDS2 6 Month Stability @ 27

STANDARD CALIBRATION CURVE

= 254 nm

Data of Average Values

dil adj

mcg/ml	AUC	AUC	AVGAUC	Hr.	mcg/ml	mcg/ml	mcg/cm2	dil	1/cm2
0	0	0	0	0.0	0.0	0.0	0.0	0.0	0.0
1	394	980	937	0.5	4.0	4.0	11.3	11.3	11.3
10	10153	10276	10215	1	5.3	5.4	15.2	4.0	4.0
25	27109	25930	26520	2	7.3	7.4	20.9	5.7	5.7
50	55408	55359	55384	4	10.0	10.1	28.6	7.7	7.7
				8	12.6	12.8	36.1	7.5	7.5
				24	14.7	14.8	42.0	5.9	5.9
				48	20.1	20.2	57.6	15.6	15.6
				72	22.3	22.6	63.8	6.3	6.3

Regression Output:

Constant -439.341
Std Err of Y Est 625.6089
R Squared 0.999452
No. of Observations 5
Degrees of Freedom 3

6 MONTH STABILITY
ROOM TEMPERATURE

Y Coefficient(s) 1107.572
Std Err of Coef. 14.96860

HR.	A cell	B cell	C cell	AVG.	STD.
0	0	0	0	0	0
0.5	4363	3911	3625	3966.333	303.3171
1	5555	5516	5277	5449.333	122.3938
2	7813	3042	7346	7668.666	286.3905
4	10256	10196	11478	10643.33	530.7065
8	13605	13908	13064	13525.66	343.9982
24	16729	14897	15762	15796	748.2971
48	21975	21373	22204	21850.66	350.4609
72	24769	23532	24337	24212.66	512.5988

Formulation Wt.%
Silver sulfadiazine 20
Chlorhexidine gluconate 10
Pluronic L-62 20
Matrix 50

Date: 05/09/91
File: SEMSTA45.WK1

ELUTION RATE WORKSHEET FOR CHLORHEXIDINE GLUCONATE "A"

TITLE : 20:10 Silver Sulfadiazine:Chlorhexidine Gluconate ADD's B.N. 010181-PPDS2 6 MONTH @ RT

STANDARD CALIBRATION CURVE

= 238 nm

				Data of Average Values				
				dil adj				
mcg/ml	AUC	AUC	AVGAUC	Hr.	mcg/ml	mcg/ml	mcg/cm2	dif u/cm2
0	0	0	0	0.0	0.0	0.0	0.0	0.0
100	692161	635665	663913	0.5	105.2	105.2	297.8	297.8
500	3130083	3112454	3121269	1	140.7	142.3	402.6	104.8
800	4897447	4849777	4873612	2	202.7	204.8	579.6	177.0
1000	6190564	6329491	6260028	4	297.5	300.5	850.4	270.8
				8	426.6	431.1	1220.0	369.6
				24	552.3	558.7	1581.1	361.1
				48	731.3	739.6	2093.0	511.9
				72	768.1	779.0	2204.6	111.6

Regression Output:

Constant 15908.43
Std Err of Y Est 65650.93
R Squared 0.999548
No. of Observations 5
Degrees of Freedom 3

6 MONTH STABILITY
ROOM TEMPERATURE

X Coefficient(s) 6183.032
Std Err of Coef. 75.90845

HR.	A cell	B cell	C cell	AVG.	STD.
0	0	0	0	0	0
0.5	708546	593068	698189	666601	52167.31
1	930053	818214	909176	885816.3	48556.36
2	1269039	1225863	1312593	1269165	35407.48
4	1896005	1783092	1886331	1855142.	51100.36
8	2777645	2469644	2714035	2653774.	132764.5
24	3495444	3155994	3640825	3430754.	203148.2
48	4619820	4415922	4576798	4537513.	87753.67
72	4910904	4537627	4845923	4764818	162823.0

Formulation Wt. %
Silver sulfadiazine 20
Chlorhexidine gluconate 10
Plaronic L-62 20
Matrix 50

Date: 05/22/91
File: CEMSTART.WK1

ELUTION RATE WORKSHEET FOR SILVER SULFADIAZINE "A"

TITLE : 20:10 Silver sulfadiazine:Chlorhexidine Gluconate ADD's B.N. 010181-PDDS2 6 Month Stability 23 C/ W

STANDARD CALIBRATION CURVE

= 254 nm

				Data of Average Values			
				dil adj			
mcg/ml	AUC	AUC	AVGAUC	Hr.	mcg/ml	mcg/ml	mcg/cm2 dif u/cm2
0	0	0	0	0.0	0.0	0.0	0.0
1	894	980	937	0.5	3.7	3.7	10.4 10.4
10	10153	10276	10215	1	5.1	5.2	14.6 4.2
25	27109	25930	26520	2	7.4	7.5	21.1 6.5
50	55408	55359	55384	4	9.5	9.7	27.3 6.2
				8	12.3	12.4	35.1 7.8
				24	14.0	14.2	40.1 5.0
				48	18.9	19.1	54.0 13.9
				72	19.5	19.8	56.0 2.0

Regression Output:

Constant -439.341
Std Err of Y Est 625.6089
R Squared 0.999452
No. of Observations 5
Degrees of Freedom 3

6 MONTH STABILITY
23 C UNDER WATER

X Coefficient(s) 1107.572
Std Err of Coef. 14.96860

HR.	A cell	B cell	C cell	AVG.	STD.
0	0	0	0	0	0
0.5	3486	4220	3228	3644.666	420.2359
1	4850	5436	5407	5231	269.6676
2	7152	8035	8033	7740	415.7795
4	9549	10684	10146	10126.33	463.5704
8	13469	13800	12161	13143.33	707.6365
24	15678	18223	11304	15068.33	2857.377
48	19521	21045	20847	20471	676.5973
72	22036	18746	22748	21176.66	1743.146

Formulation
Silver sulfadiazine
Chlorhexidine gluconate
Plaronic L-62
Matrix

Wt. %
20
10
20
50

Date: 05/15/91
File: SEMSTANT.WK1

ELUTION RATE WORKSHEET FOR CHLORHEXIDINE GLUCONATE "A"

TITLE : 20:10 Silver Sulfadiazine:Chlorhexidine Gluconate ADD's B.N. 010181-PPDS2 6 MONTH @ 23C/WATER

STANDARD CALIBRATION CURVE

= 238 nm

				Data of Average Values				
				dil adj				
mcg/ml	AUC	AUC	AVGAUC	Hr.	mcg/ml	mcg/ml	mcg/cm2	dif u/cm2
0	0	0	0	0.0	0.0	0.0	0.0	0.0
100	692161	635665	663913	0.5	80.7	80.7	228.5	228.5
500	3130083	3112454	3121269	1	124.8	126.0	356.6	128.1
800	4897447	4849777	4873612	2	188.2	190.1	537.3	181.3
1000	6190564	6329491	6260028	4	286.5	289.3	818.7	280.8
				8	423.3	427.6	1210.2	391.5
				24	606.2	612.5	1733.5	523.3
				48	685.8	694.9	1966.6	233.1
				72	689.9	700.2	1981.5	14.3

Regression Output:

Constant	15908.43	6 MONTH STABILITY
Std Err of Y Est	65650.93	23 C UNDER WATER
R Squared	0.999548	
No. of Observations	5	
Degrees of Freedom	3	

X Coefficient(s) 6183.032

Std Err of Coef. 75.90845

HR.	A cell	B cell	C cell	AVG.	STD.
0	0	0	0	0	0
0.5	444615	533168	567477	515086.6	51762.07
1	722698	804295	835640	787544.3	47605.40
2	1132859	1277463	1128383	1179568.	69246.09
4	1685726	1924886	1750713	1787108.	100971.4
8	2423399	2966011	2510888	2633432.	237865.2
24	3587015	4159009	3546150	3764058	279770.3
48	3964894	4548761	4255231	4256295.	238363.3
72	4168673	4548004	4127929	4281535.	189154.5

Formulation Wt. %
 Silver sulfadiazine 20
 Chlorhexidine gluconate 10
 Pluronic L-62 20
 Matrix 50

Date: 05/22/91
 File: C6MSTANT.WK1

ELUTION RATE WORKSHEET FOR SILVER SULFADIAZINE "A"

TITLE : 20:10 Silver sulfadiazine:Chlorhexidine Gluconate ADD's B.N. 010181-PDDS2 6 Month Stability -40 C

STANDARD CALIBRATION CURVE

= 254 nm

				Data of Average Values			
				dil adj			
mcg/ml	AUC	AUC	AVGAUC	Hr.	mcg/ml	mcg/ml	mcg/cm2 dif u/cm2
0	0	0	0	0.0	0.0	0.0	0.0
1	894	980	937	0.5	3.8	3.8	10.7
10	10153	10276	10215	1	4.2	4.3	12.2
25	27109	25930	26520	2	5.9	6.0	16.9
50	55408	55359	55384	4	6.7	6.8	19.3
				8	7.6	7.7	21.7
				24	10.7	10.8	30.5
				48	13.7	13.8	39.1
				72	13.7	13.9	39.3

Regression Output:

Constant	-439.341	6 MONTH STABILITY
Std Err of Y Est	625.6089	-40 C
R Squared	0.999452	
No. of Observations	5	
Degrees of Freedom	3	

X Coefficient(s) 1107.572

Std Err of Coef. 14.96860

HR.	A cell	B cell	C cell	AVC.	STD.
0	0	0	0	0	0
0.5	4459	2535	4195	3729.666	851.6044
1	4533	4087	4149	4256.333	197.2635
2	5893	6074	6376	6114.333	199.2357
4	7748	7343	5929	7006.666	779.7565
8	9069	6692	8122	7961	977.0612
24	14519	3713	3897	11376.33	2323.470
48	15948	16874	11246	14639.33	2463.977
72	11812	19031	13307	14716.66	3111.147

Formulation	Wt. %
Silver sulfadiazine	20
Chlorhexidine gluconate	10
Pluronic L-62	20
Matrix	50

Date: 05/09/91
File: S6MSTA45.WK1

ELUTION RATE WORKSHEET FOR CHLORHEXIDINE GLUCONATE "A"

TITLE : 20:10 Silver Sulfadiazine:Chlorhexidine Gluconate ADD's B.N. 010181-PPDS2 6 MONTH @ -40C

STANDARD CALIBRATION CURVE

= 238 nm

Data of Average Values
dil adj

mcg/ml	AUC	AUC	AVGAUC	Hr.	mcg/ml	mcg/ml	mcg/cm2	dif u/cm2
0	0	0	0	0.0	0.0	0.0	0.0	0.0
100	692161	635665	663913	0.5	75.7	75.7	214.2	214.2
500	3130083	3112454	3121269	1	109.9	111.0	314.2	100.1
800	4897447	4849777	4873612	2	172.6	174.2	493.0	178.8
1000	6190564	6329491	6260028	4	258.7	261.3	739.4	246.4
				8	355.5	359.4	1017.0	277.6
				24	499.3	504.7	1428.2	411.1
				48	616.7	624.2	1766.3	338.2
				72	666.6	675.9	1912.7	146.3

Regression Output:

Constant	15908.43	6 MONTH STABILITY
Std Err of Y Est	65650.93	-40 C
R Squared	0.999548	
No. of Observations	5	
Degrees of Freedom	3	

Y Coefficient(s) 6183.032

Std Err of Coef. 75.90845

HR.	A cell	B cell	C cell	AVG.	STD.
0	0	0	0	0	0
0.5	430592	541263	479733	483864.6	45275.33
1	635802	836985	613601	695462.6	100481.0
2	1016469	1213339	1018920	1082909.	92233.12
4	1501246	1827199	1517610	1615351.	149947.5
8	2244228	2427895	1969804	2213975.	188234.3
24	3548582	3047262	2713832	3103225.	343075.1
48	3955589	4328524	3202116	3828743	468519.7
72	4134969	4581666	3696127	4137587.	361524.5

Formulation Wt. %
Silver sulfadiazine 20
Chlorhexidine gluconate 10
Pluronic L-62 20
Matrix 50

Date: 05/20/91
File: CGMSTA40.WK1