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Quality Control study of Silver and Chlorohexidine Wound Dressings: A Comparison of Physical and Chemical Characteristics of Some Types Available in Middle East Medical Supply

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ABSTRACT

Objectives: Antibacterial dressings are widely used to assist with management of infected wounds and those at risk of infection. However, such dressings have varied responses in clinical use due to technological differences in the nature of their antibacterial content and release and in properties of the dressings themselves. This study is focusing on two types of antibacterial dressings widely used in Middle East which are Chlorohexidine and Silver dressings. **Methods:** In this study we examined the physical and chemical parameters related to quality of the dressing for seven different product types of the two mentioned antibacterial dressings. **Results:** showed the relationship between the antibacterial content, rate of its release, and expected antibacterial action based on their reported minimum inhibitory concentrations (MICs). It also looked at other important measures for the clinical performance of dressings including fluid handling properties and dressing pH. **Conclusion:** the choice of an appropriate antibacterial dressing should be based on the wound type, condition and on clinically applicable measures, such as antibacterial, healing, and exudate handling effects, and not on any single laboratory parameter.

Keywords: *Chlorohexidine, Middle East, Medical supply, Silver, Quality control, Wound dressing*

INTRODUCTION

The skin covers our entire body and acts as a barrier between the outside and inside environment to help maintain body's temperature and fluid/electrolyte balance. A wound is a discontinuity of the skin, mucous membrane or tissue caused by physical, chemical or biological insult. The warm, moist environment on the wound surface, together with a ready supply of nutrients, offers an ideal setting for bacterial proliferation. Infections, either by bacteria or fungi, can cause great pain, lead to deterioration of the wound healing process and severe systemic complications. Wound dressings containing topical antimicrobial agents, such as Chlorohexidine and silver; have provided a new approach to the control of wound pathogens.[1]

Chlorohexidine acetate is a biguanide, which is less toxic to tissues and has high antimicrobial activity against both gram positive and gram negative bacteria and some fungi and viruses. It has antibacterial activity in the presence of blood, pus and other organic debris and low systemic absorption and toxicity.[2]

Silver has wide applications as antiseptic in wound dressing due to its broad spectrum antimicrobial

activity [3] with minimal toxicity toward mammalian cells at low concentrations [4] and has a less likely tendency than antibiotics to induce resistance due to its activity at multiple bacterial target sites.[5]

This study compares physical and chemical parameters of seven antibacterial dressings; three of chlorohexidine and four of silver impregnated dressing. The correlation between antimicrobial content and/or its release from each dressing and its expected antibacterial effect is examined, and factors relating to the provision of an optimal environment for wound healing are compared to provide a basis for an overall assessment of the clinically valuable properties of each dressing.

MATERIALS AND METHODS

This study evaluate Dressing sample materials which are collected from Saudi medical supplies: three chlorohexidine dressings (Bactigras®, Cuticell™ C and Damad antiseptic dressing), and four silver dressing (Acticoat, Aquacel Ag, Exsalt™ SD7 and Medifoam S). The investigated dressings vary in their components and structures which can be summarized in table 1.

Standards and Reagents

During analysis reference materials used are standard chlorohexidine diacetate powder [(Eu. Parma), sigma number (56-95-1)] and standard silver nitrate solution 1000 ppm in 2% HNO3 of lot number AG010609 (HORIBA JOBIN YVON). Other reagents used are of analytical grade, hydrochloric acid 37% (Scharlau), Nitric acid pure 69-72% (Art. 223) and Sulphoric acid 98% (ARBUDA). Cetrimide (BDH) GPR TM Prod 276654L, Bromine water (Hushi) 2001001 Analytical grade [7726-95-6]. Double distilled water was obtained through Nanopure II water purification system (Barnstead/ Thermolyne, Dubuque, IA, USA) and used through the work. Also deionized water was used through the atomic absorption measurements.

Apparatus

For spectrometric analysis of chlorohexidine, the measurement is done on double beam V-530 ultraviolet-visible spectrophotometer (JASCO Co. Ltd., Kyoto, Japan), with matched 1-cm quartz cells. For atomic absorption, the measurement of silver atomic absorption performed on GBC 906 Savanta atomic absorption spectroscopy with HG3000 pump. The light source used is Ag hollow cathode lamp GBC (HHH0961) of wave length 328.1 nm. For pH determination, the measurement is done by Mettler Toledo pH meter MP 220. The hot plate used for heating and digestion of the matrix was Barnstead 1 Thermolyne Cimarec.

Measurement of physical parameters

A. Chlorohexidine dressings

1. Threads per 10 cm

We randomly select 5 samples of each type of the dressing with the size 10 x10 cm. Then we visually count the threads of the unstretched dressing over the two sides of the square gauze.

2. Weight per unite area

The sample is weighed (w). Its unstretched width (a cm) and length (b cm) are measured. Then the weight per unite area is calculated in gm\ m^2 from the expression.

$$\text{Weight per unite area} = \frac{w \times 10000}{a \times b}$$

B. Silver dressing

Fluid handling properties

1. Weight of fluid absorbed per gram of the dressing

The four investigated silver dressings Acticoat, Aquacel Ag, Exsalt ™ SD7 and Medifoam S are studied for the fluid absorption features of their matrices. A sample of dressing of size 2.5x 2.5 cm is weighed in dry state and placed in salt solution contains 142 mmol/L sodium ions and 2.5 mmol/L calcium ions, values typical of those found in serum and wound fluid.[6] Then the change in the weight of the sample is recorded after 30 minutes, 1 hour and 24 hours in order to determine the increase in weight of the dressing due to absorbing fluid. The weight of fluid absorbed and retained per gram of the dressing within 1 hour is calculated by $(W_2 - W_1)/W_1$. As W_1 is the weight of the dressing before the test and W_2 is the weight after absorbing the fluid for 1 hour.

2. Volume of fluid absorbed per 10cm2 per 24 hours

The reported value of the produced fluid by the moderately to highly exuding wounds is approximately 5ml per $10cm^2$ per 24 hours [7]. The total volume of the absorbed water during 24 hour is determined by the reduction in the volume of initially added 20 ml salt solution as a result of insertion of 2.5x 2.5 cm dressing piece for 24 hour. Then the volume of the fluid absorbed per $10cm^2$ per 24 hours is calculated.

Measurement of chemical parameters

A. Chlorohexidine dressings

1. Content of antiseptics

a. Standards, preparations and reagents

The calibration curve is drown from serial dilutions of 0.01% w/v of standard chlorohexidine diacetate solution in a mixture of 1M HCl and distilled water by ratio 5:95. The reaction is done on the standers as in official method. The linear range was obtained from (0.001%-0.006% w/v) solutions.[8]

Table 1: Investigated Chlorhexidine acetate and silver dressings, their manufacturers and product specifications

	Trade Name of the product	Active ingredient and concentration	Manufacturer	Product type and formula description
1	**Bactigras®**	Chlorhexidine acetate BP 0.5% w/w	Smith & Nephew (UK) http://wound.smith-nephew.com	Tulle grass (a medicated paraffin gauze dressing)
2	**Cuticell ™ C**	Chlorhexidine acetate BP 0.5% w/w	**BSN** medical (India) www.bsnmedical.com	Tulle grass (a medicated paraffin gauze dressing)
3	**Damad antiseptic dressing**	Chlorhexidine acetate BP 0.5% w/w	Saudi National medical products http://www.damad.com	Tulle grass (a medicated paraffin gauze dressing)
4	**Acticoat 7**	Nanocrystalline silver. The Nanocrystal coating contains 1.05 mg silver/cm^2. The silver coating consists of 0.25±0.4 mg silver per mg of the high-density polyethylene net. The content of silver coated layer is 99.99% silver.	Smith & Nephew (UK) http://wound.smith-nephew.com	Three-ply gauze dressing consisting of an absorbent polyester inner core sandwiched between outer layers of silver-coated, polyethylene net (nanocrystalline silver) The nanocrystalline silver placed onto a bilayer of polyethylene provides an initial large bolus of silver to the wound followed by a subsequent, more sustained release.
5	**Aquacel Ag**	Silver-impregnated dressing with hydrofibre composed of Hydrocolloid and 1.2% w/w (0.083 mg /cm^2) ionic silver. Silver ions are slowly released from the carrier as it is hydrated, thereby achieving a gradual and sustained release for up to 2 weeks.	ConvaTec (U.S.A) http://www.convatec.com	Sodium carboxy methylcellulose hydrofiber. It is a moisture-retention dressing, which forms a gel on contact with wound fluid and has antimicrobial properties of ionic silver. The dressing entraps microorganisms within its fibers. Then controlled release of silver ions reduces the bioburden within the dressing and minimizing the risk of infection.
6	**Exsalt ™ SD7**	Oxidized silver species incorporated onto non-woven needled polyester coated with gray mesh layers on both sides. The concentration of the silver and oxidized silver species on the dressing is 0.4 mg/ cm^2 (2.5% w/w).	Exciton Technologies (Canada) www.excitontech.com	2 outer layers of high-density polyethylene (HDPE) with an inner layer of absorbent polyester which are all silver-coated.
7	**Medifoam S**	Contains regular distribution of Silver suphadiazine (AgSD) concentration : 125µg/cm^2	Biopol (Korea) http://biopolglobal.en.ec21.com/	Polyurethane foam with controlled release of the antibacterial drug (AgSD) to the foam.

The colored product for the quantitative analysis is produced by reacting 40 ml of the prepared standard solution with 2 ml of 1% v/v bromine solution in 10M NaOH in presence of 5 ml of 20% w/v solution of cetrimide as a surfactant to prevent precipitation. The reaction is done in alkaline medium. 1ml of propan-2-ol is added to suppress the froth. Then the volume is completed to 100 ml by distilled water and the product is allowed to stand for 25 minutes before measuring the absorbance of the resulting solution at 480 nm.[8]

b. Dressing sample solution preparation

According to the British Pharmacopeia[8] in determination of antiseptic contents, 30 g of the dressing was shaken several times with several portions of a mixture of distilled water and 1 M HCl by the ratio of 7:3 to extract the chlorohexidine in the aqueous extract. Then to 40 ml of that solution, 45 ml of water and 5 ml of 20% cetrimide solution were added. The mixture was shaken and 2ml of 1% bromine solution in 5 M NaOH is then added. 1ml of alcohol is added to suppress the froth then the volume is completed to 100 ml with water.

As a result, a red color is developed which is measured spectrometrically at 480 nm after standing for 25 minutes to complete the reaction. The sample concentration is calculated from the calibration curve or from the regression equation.

2. pH of the dressing

One dressing pad (in duplicate) from each dressing were suspended in 50 ml of distilled water and incubated at 37°C to simulate the body temperature. Then the pH was measured after 1 hour, 2 hours and 24

hours using a pH meter with a combination pH electrode, calibrated at pH 4 and 7.

3. Chlorohexidine release into water over time

One dressing pad (in duplicate) from each dressing was suspended in 50 ml distilled water. The samples were placed into a temperature controlled environment (37.0 ± 3°C) for 1 day. During this period, aliquots were removed after 1 hour, 2 hours and 24 hours ,the liquid was replaced to maintain a constant volume. From aliquots 10 ml is taken and the reaction is done keeping the ratio of the reagents as indicated in the official method[8] the absorbances of the products are recorded as mentioned before and from which the concentrations are calculated.

B. Silver dressing

1. Measurement of total silver content

a. Standards, preparations and reagents

For silver analysis the calibration curve is drawn from serial dilutions of the standard silver nitrate 1000 ppm. The linear range for silver analysis was obtained from 1.4 -5 ppm at wavelength 328.1 nm and the dilution to that range was done by de-ionized water.

b. Dressing sample solution

For determination of silver content in the dressing pad, the pad is digested in a mixture of H_2SO_4 and HNO_3 by a ratio of 1:4 with boiling on a hot plate in a hood until the matrix is completely digested. After complete digestion of the matrix the content is transferred to 50 ml volumetric flask with completing to the mark by deionized water. Then the solution is centerfugated for 5 minutes in 3000 rpm to take the clear supernatant. A serial dilution of the clear part is then taken to 25 ml volumetric flask and diluted to volume by deionized water in order to adjust the sample concentration to be in linear range of the quantization of atomic absorption at 328.1 nm. The sample concentration is calculated from the calibration curve or from the regression equation.

2. pH of the dressing

Samples (in duplicate) from each dressing were suspended in deionized water at a ratio of 1:100 (w/v) and incubated at 37 ±3 ^{0}C. The pH of the extract was measured using a calibrated pH meter after 2 hours and 24 hours.[9]

3. Silver release into water over time

As described by Parsons, *et. al.* [9] a weighed portion (in duplicate) from each dressing was suspended in deionized water at a ratio of 1:100 (w/v), and the samples were placed into a temperature-controlled environment (37.0 ± 3°C). During 2 days period, aliquots were removed at 30 minutes, 3 hours, 24 hours and 48 hours, and the liquid was replaced to maintain a constant volume. Samples were filtered, diluted as appropriate, and analyzed by atomic absorption spectrometry.

RESULTS AND DISCUSSION

Measurement of physical parameters

A. Chlorohexidine dressings

British Pharmacopeia[8], specifies some parameters in testing and evaluating the surgical dressing materials including:

1. Threads per 10 cm

This test is done to reflect loading efficiency of the dressing. The number of threads per 10 cm are counted and reported in table 2

In our samples we have found that the threads are squared then we suggest to use 77 as the Pharmacopeial standard for our squared samples. The statistical student T test, shows that there is a significant difference between the average number of threads in the three types with the standard value of 77 (P-value < 0.05) to the favor of the standard value.

2. Weight per unite area

Weight per unite area is calculated with reference to British Pharmacopeia.[8]

Form table 3, we deduced that our samples are presented as single pack and all their values are within the standard range. In addition, the coefficient of variation shows that Bactigras dressing is the most homogenous loaded, while Damad has more variations. This may refer to uploading machine.

B. Silver dressing

Fluid Handling Properties

Most dressings are designed to absorb exudates, lock it in and therefore hold it away from the wound bed and the surrounding skin.

1. Weight of fluid absorbed per gram of the dressing

The results of the free swell fluid absorption parameters, without applying pressure, are shown in table 4. For clear comparison, figure 1 shows the weight change over the time as a result of fluid absorption.

From table 4 we can calculate the weight of fluid absorbed and retained per gram of the dressing. We find that Aquacel Ag absorbs 33.4 gm fluid per gram of dressing within 1 hour. Exsalt absorbs 0.73 gm/gm fluid within 1 hour. Acticoat and Medifoam S absorb 8.5 gm/gm and 9.7 gm/gm respectively within 1 hour. The value is greatest for the hydrofiber Aquacel Ag and least for Exsalt while Acticoat and Medifoam are similar even that the value of Medifoam expected to be high as it has foam matrix.

Table 2: Threads per 10 cm of the Chlorohexidine dressing samples

Product	Sample 1	Sample 2	Sample 3	Sample 4	Sample 5	Average	t- test	P-value
Bactigras®	54	53	55	53	55	54	51.4	> 0.05
Cuticell ™	54	55	53	54	53	53.8	62.0	> 0.05
Damad	39	41	43	42	43	41.6	47.3	> 0.05

$T_{tab.}$ (P- value 0.05) = 5.841

Pharmacopeial monograph stated that the number should be not less than 74 at warp and not less than 80 at weft.

Table 3: Weight per unit (gm/m^2) area of the Chlorohexidine dressing samples

Product	W1	W2	W3	W4	W5	Avg. w	Coefficient of Variation %
Bactigras®	198	203	194	206	196	199.4	2.5
Cuticell ™	216	234	230	244	231	231.0	4.4
Damad	194	250	245	199	200	217.6	12.6

Pharmacopeia stated that for impregnated fabric light loaded the weight per unit area is 100 to 125 gm\ m^2. While the normal loaded it should be not less than 200 gm\ m^2 and when presented as single pack, not less than 175 gm\ m^2.

Table 4: Absorbance capacity data of the silver dressing types

Product name	Sample Weight Before test (gm)	Sample Weight After 30 min. (gm)	Sample Weight After 1 hour (gm)	Sample Weight After 24 hour (gm)	weight of fluid retained/gram of dressing within 1h	Volume. absorbed after 24 hour (ml)
Aquacel Ag	**0.058**	**1.57**	**1.995**	gel cannot be handled	**33.4 gm/gm**	**5**
Exsalt ™SD7	**0.103**	**0.138**	**0.178**	**0.331**	**0.73 gm/gm**	**2.5**
Acticoat	**0.064**	**0.664**	**0.608**	**0.655**	**8.5 gm/gm**	**2.75**
Medifoam S	**0.809**	**8.71**	**8.61**	**8.775**	**9.7 gm/gm**	**11.5**

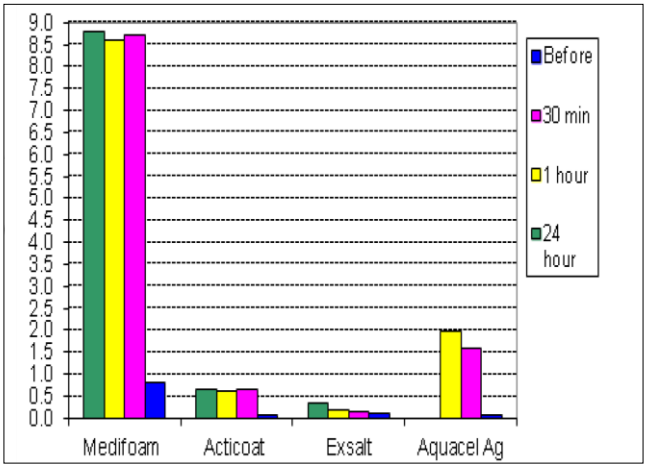

Figure 1: Weight change that reflect absorption feature of the investigated Ag dressings

2. Volume of fluid absorbed per 10cm^2 per 24 hours

By calculating the volume absorbed from the data in table 4 we can conclude that, as the foams, alginates and hydrofiber are suggested to be suitable for highly exuding wounds, the volume retained within Aquacel Ag and Medifoam S in 24 hours should be ≥ 5ml/ 10cm^2 / 24 hours. By calculation we find that Aquacel Ag retains 8 ml/10cm^2/24 hours which indicates that its capacity to retain fluids is higher than that produced by heavily exudating wounds. Medifoam S retains 18.4 ml/10cm^2/24 hours so it is suitable for heavy exudates as told in its indication for use. Exsalt™ and Acticoat retain 4 ml/10cm^2/24 hours and 4.4 ml/10cm^2/24 hours respectively. The registered indication of those two dressings says that they are not suitable for heavy exudate which is proved by the experiment.

Taking in mind that the dressing must be able to handle the exudate and retain it even under pressure due to the presence of secondary dressing such as compression bandage.

Figure 2 shows that, the increase in the weight of the dressing due to fluid absorption within the 1st hour, is the maximum for Aquacel Ag and minimum for Exsalt while Medifoam S and Acticoat are nearly similar. But based on the volume absorbed within 24 hours Medifoam S is the maximum while Acticoat and Exsalt are the least and nearly similar. So we can conclude that the fluid retention power of the hydrofiber is based on weight not volume because the dressing is very fluffy and has low weight compared with the other types while for foam dressing the fluid retention power is mainly volume because the dressing originally has the highest weight so if increase in weight happened it will be uncomfortable to wear on the wound sit.

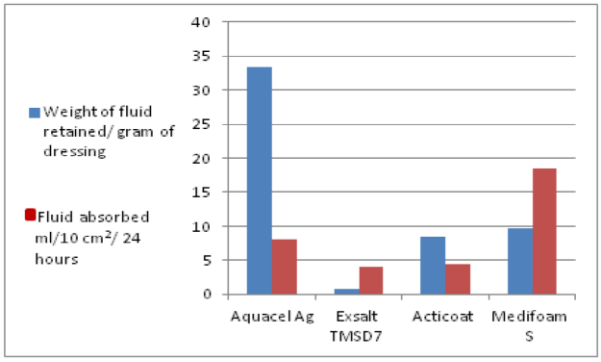

Figure 2: Comparison between weights of fluid retained per gram of Ag dressing within 1h and volume absorbed after 24 hour

Measurement of Chemical Parameters

A. Chlorohexidine dressings

1. Content of antiseptics

Figure 3 shows the absorption spectrum of chlorohexidine before and after the reaction with Bromine. The results and calibration curve of the standard chlorohexidine solution reaction product is shown in table 5 and figure 4.

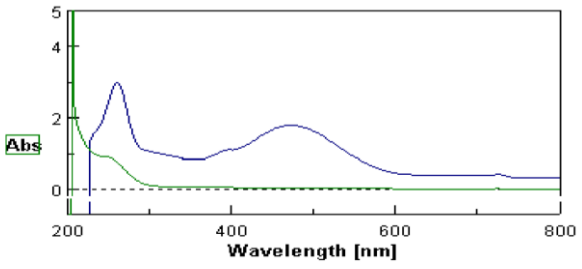

Figure 3: Absorption spectra of Chlorohexidine before and after the reaction with Bromine

Table 5: The concentrations against absorbencies of standard Chlorhexidine acetate solutions

Conc. g % w\v	A1	A2	A3	A4	Mean A
0.001	0.114	0.149	0.157	0.121	0.13525
0.002	0.237	0.242	0.262	0.265	0.2515
0.003	0.401	0.402	0.426	0.430	0.41475
0.004	0.585	0.588	0.606	0.605	0.596
0.005	0.706	0.712	0.718	0.719	0.71375
0.006	0.921	0.923	0.918	0.916	0.9195

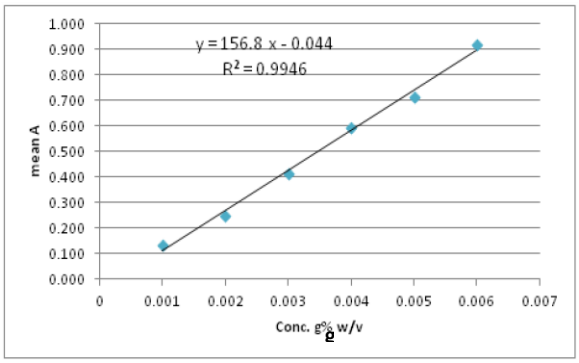

Figure 4: Calibration curve for standard Chlorhexidine acetate solutions. The regression equation is: Y= 156.8X - 0.044 (r^2=0.995) Where Y is the absorbance and X is the concentration in gm%

The content of chlorhrxidine in the three investigated chlorohexidine impregnated pads, Bactigras®, Cuticell ™ and Damad antiseptic dressing was determined from the regression equation of the standard and by calculating the content; the percentage recoveries of the products are calculated as the labeled concentration for them all is 0.5%w/w and listed in table 6.

2. pH of the dressing

Measurement of dressing pH obtains the results stated in table 7. Dressing pH was measured to provide an indication of how the surface of a dressing changes when wet. It has been suggested that dressings with a slightly acidic pH (similar to that of healthy skin; pH of 5.5) may be most comfortable to wear. There have been reports, however, of some dressings causing irritation or stinging after absorbing exudate, suggesting that a change in dressing pH may be occurring. [9] But as mentioned before Chlorhexidine exhibits the greatest antibacterial activity at pH 7–8 where it exists as a dication. [10] The observations showed that all the pH

Table 6: The absorbencies (A) of the product Chlorhexidine contents and its percentage recovery

Product	Lot #	A1	A2	A3	A4	Average of A	% recovery	95% C.I.* for the mean of A
Bactigras®	105	0.824	0.799	0.820	0.799	0.811	92%	(0.789,0.832)
Cuticell ™	cc-1105	1.088	1.162	1.147	1.102	1.125	124%	(1.069,1.181)
Damad	9152G0001	0.785	0.731	0.788	0.733	0.759	84.33%	(0.709,0.809)

* Confidence interval

Table 7: Chlorhexidine dressing pH in distilled water

Product	pH after 1 hour	pH after 2 hours	pH after 24 hours	Coefficient of variation
Bactigras®	5.81	6.21	6.13	3.5
Cuticell ™	6.06	6.41	5.96	3.8
Damad	5.99	7.31	4.89	20.0

Table 8: Data for chlorohexidine release

Product name	Average sample weight 10X10 cm	Conc. released after 1h (mg/gm)	Conc. released after 1h (µg/ml)	Conc. released after 2h (mg/gm)	Conc. released after 2h (µg/ml)	Conc. release after 24h (mg/gm)	Conc. released after 24h (µg/ml)
Bactigras®	2.04	0.123	5.03	0.192	7.82	0.280	11.44
Cuticell ™	2.33	0.135	6.30	0.190	8.84	0.243	11.35
Damad	2.65	0.064	3.40	0.127	6.73	0.243	12.94

values of the dressings are in the range of 4.9 to 7.5 which may be comfortable to wear. Bactigras and Cuticell showed more stable pH over the time than Damad antiseptic dressing, whose pH change markedly in the 1st two hours indicating that some form of chemical reaction may be taking place, but both of Bactigras and Cuticell do not reach the optimum pH for antibacterial activity. Damad antiseptic dressing is the only one reach the optimum antibacterial pH but after 2 hours.

3. Chlorohexidine release into water over time

The concentrations per weight of the pad (mg/gm) and the concentration of the released chlorohexidine (µg/ml) over the time of the three products are summarized in table 8. The MIC of chlorhexidine ranged from 2.67 to 80.00 µg/ml. The highest MIC values of chlorhexidine were observed for *P. aeruginosa* whereas *E. coli* and *P. denticola* were the most susceptible microorganisms to this agent [11]. From the results above we said that during the 1st hour of application all the three dressing types release the antibacterial level of the drug. The level of the drug still in the antibacterial range over the time for 24 hour, the time expected to change the dressing. But the concentration of the drug released from those formulae within the 24 hour is not effective on *P. aeruginosa*.

concentration of the drug released from those formulae within the 24 hour is not effective on *P. aeruginosa*.

Figure 5 shows the behavior of the release measured after 1 hour, 2 hours and 24 hours, respectively. As it shows that the amount of Chlorohexidine released after 1 hour for the Cuticell is larger than the other two products while the amount of Chlorohexidine released after 2 hour for the Cuticell and Bactigras are almost equal. After 24 hours we see that Bactigras is almost the largest one. In all cases Damad has the smallest release over the time; this is expected since the content of medication in Damad is the smallest.

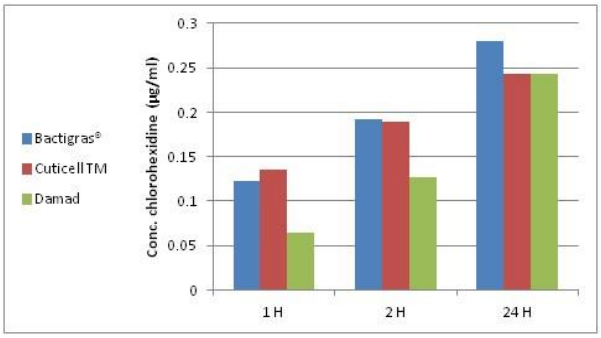

Figure 5: The behavior of the Chlorohexidine dressing pads release based on time

Figure 6 shows that, all the pads have gradual increase in release over the time. The rate of change from the dressing pad release from 1 to 2 hours is 55.6%, 40.3%, 88.1% for Bactigras, Cuticell and Damad respectively. This shows that Cuticell is the most stable in release over the time among the other two. While Damad is the most changeable and this is clear in figure 7.

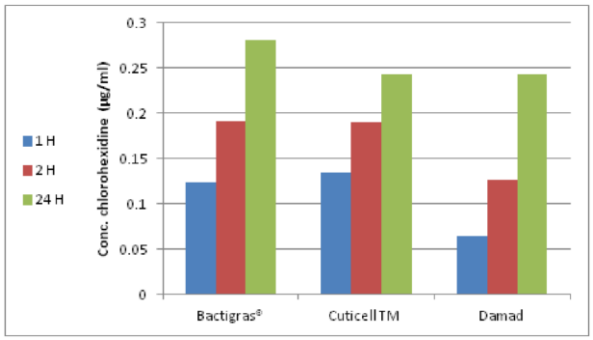

Figure 6: Bactigras, Cuticell and Damad dressing pads release

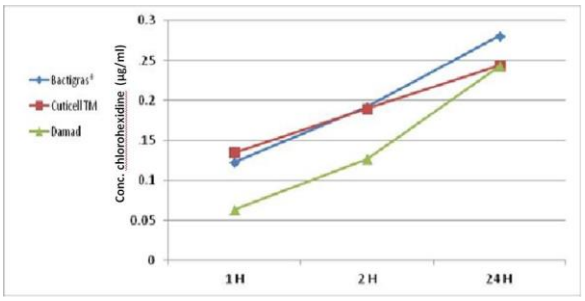

Figure 7: Bactigras, Cuticell and Damad dressing pads release

B. Silver dressing

1. Atomic absorption measurement of total silver content

The concentrations against atomic absorbance of the serial dilutions of the standard silver solution are measured and the results are shown in table 9.

Table 9: Concentrations of standard silver and their atomic absorbance

Standard	conc. ppm	A1	A2	A3	mean Abs.
1	1.5	0.269	0.277	0.334	0. 293
2	2	0.360	0.358	0.357	0. 358
3	4	0.566	0.573	0.583	0. 574
4	5	0.734	0.729	0.717	0. 726

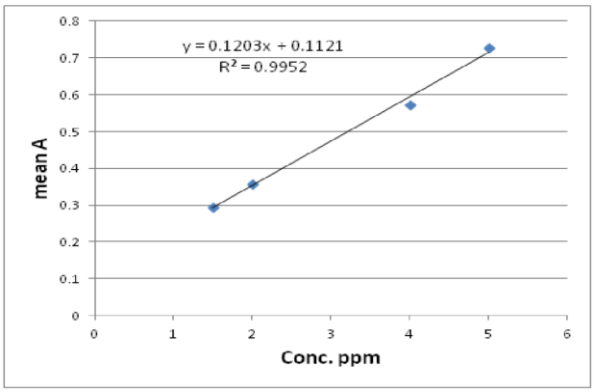

Figure 8: Calibration curve for standard silver solutions. The regression equation is: Y = 0.1203X + 0.1121 (r^2 =0.995), where Y is the absorbance and X is the concentration in ppm

As mentioned in the experimental part, the extracted sample solution is diluted to adjust the result within the linear rang of the atomic absorption spectrometric analysis. For silver sulphadiazine (Medifoam S), the Pharmacopeia[12] stated that the content of silver is not less than 29.3% and not more than 30.5% of the total silver sulphadiazine concentration which is 125 µg /cm^2 that means it contain about 37.4 µg silver/ cm^2 of the dressing. The calculated concentrations and percentage recoveries can be shown in the table 10.

2. pH of the dressing

Measuring the dressing pH and it stability with the time reflects the skin comfortability. The result is listed in table 11.

Table 11 shows that Aquacel Ag is the most comfortable to wear as its pH is closer to skin pH (5.5). Acticoat and Aquacel Ag are the most stable pH over the time appearing from the lower coefficient of variation compared with the other types. Exsalt is the least stable pH over the time appearing from the highest coefficient of variation.

3. Silver release into water over time

The ideal wound fluid concentration of silver for greatest antimicrobial efficacy, with levels of between 20 ppm and 60 ppm.[4] Also the bioactive form of silver is the Ag^+ ions which must be released to the tissue in sufficient concentration. Otherwise microbes should be absorbed into the dressing to encounter silver in a sufficient concentration. The used method of analysis, atomic absorption, cannot differentiate between the active ionic form and the inactive atomic form of silver. Table 12 shows the released concentrations of silver from the investigated products.

Table 10: The silver content and recoveries of the dressing samples (5 × 5 cm)

product	Average weight of 5x5 cm pad (g)	Contents of silver (mg /5x5 cm pad)	Labeled Ag contents (mg/5x5 cm pad)	% w/w of silver in the pad	% recovery
Acticoat	0.28	28.04	27.25	10%	102.9%
exsalt	0.42	8.71	10	2%	87.1%
Aquacel Ag	0.25	2.1	2.9	0.85%	72.4%
Medifoam S	2.92	1.12	0.94	0.038%	119.15%

Table 11: Silver dressing pH and its stability over time

The product	pH after 2 hours	pH after 24 hours	Coefficient of variation
Acticoat	6.57	6.96	4.1
Exsalt	5.72	6.37	7.6
Aquacel Ag	5.84	5.49	4.4
Medifoam S	6.01	6.5	5.5

Table 12: A comparison of silver content and rate of silver release

Product name	Ag Content (mg/5 x 5 cm)	Conc. Released after 1/2h (ppm)	Conc. Released after 3h (ppm)	Conc. Released after 24h (ppm)	Conc. Released after 48h (ppm)	Coefficient of variation of the release
Acticoat	28.04	17.782	20.635	70.455	78.178	68.4
Exsalt	8.71	15.593	22.86	126.152	199.052	96.8
Aquacel Ag	2.1	0.064	0.138	0.163	0.172	36.5
Medifoam S	1.12	0.083	0.203	0.486	0.711	76.3

Table 12 and figure 9 show that, none of the four types release the antimicrobial silver concentration within half an hour. After 3 hours, only Acticoat and Exsalt silver release, reach the antimicrobial level taking in mind that Acticoat release atomic Ag0 in a nano-size which is inactive form except if it is oxidized to the active Ag+.

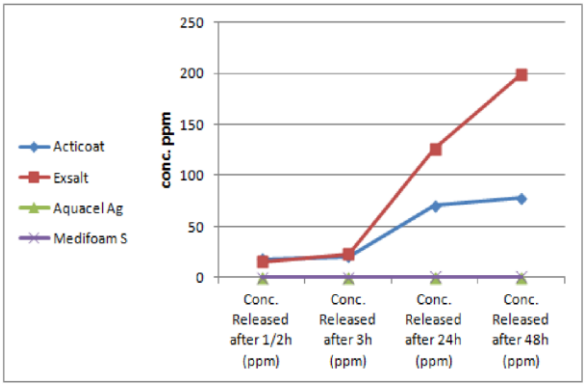

Figure 9: Ag releasing profile for Acticoat, Exsalt, Aquacel Ag and MedifoamS over time intervals

The released silver concentration from Exsalt is jumped markedly after 24 and 48 hours and become above the active level. While Acticoat release is more stable over the time for 24 and 48 hours represent the steady sustained release character of the nanocrystal drug. Aquacel Ag and Medifoam S silver release to water does not reach the antimicrobial level as observed from the results of analysis this is may be due to:

- Aquacel Ag works by absorbing the microbes into the dressing where they suffer from high silver concentration (about 84 µg/cm^2) without dilution.
- Medifoam S active ingredient is silver sulphadiazine (AgSD) in which the antibacterial effect of silver is enhanced by the synergetic effect of sulphadiazine antibiotic so less concentration is needed for bactericidal action.
- The antimicrobial activity of Silver sulphadiazine is reported as its MIC is in the range 16-64 ppm[13]. From which the level of silver range 4.7- 19.5 ppm. Again the observed silver release to water is less than that concentration because Medifoam with foam matrix highly absorbs the exudates together with the microbes into the dressing. Inside the dressing matrix

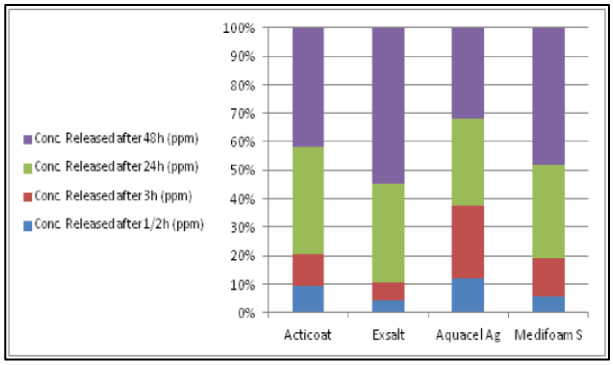

Figure 10: Comparison between Ag release percentages over time intervals

no dilution occurs and the silver concentration is 44 µg/cm^2 by which the MIC is definitely reached.

Figure 10 shows that Aquacel Ag gives the highest percentage release in first half hour and 3 hours, while Exsalt gives the lowest percentage. After 24 hours, all products give almost the same percentages. 48 hours later, Exsalt gives the highest release percentage. In terms of release stability we see that the Aquacel Ag is the most stable product and deduced from coefficient of variation in table 12.

CONCLUSION

In this study, the physical and chemical properties of wound dressing are investigated based on some products available in Middle East of medical supply namely; Bactigras® (Chlorhexidine impregnated, Smith & Nephew), Cuticell ™ C (Chlorhexidine impregnated, BSN medical), Damad antiseptic dressing (Chlorhexidine impregnated, Saudi National medical products), Acticoat (Nanocrystalline silver, Smith & Nephew), Aquacel Ag (Combined antibacterial silver dressing with hydrofiber technology, Conva Tec), Exsalt ™ SD7 (Silver coated polyethylene mesh, Canada), and Medifoam S (Silver sulphadiazine impregnated polyurethane foam, Biopol).

Thus, it could be conclude from the results of the current study, the recognition of the different dressing products available of the two antibacterial drugs under interest and their manufactures and specifications, summarizing the Pharmacopeia guidelines related to our study and reviewing the methods of analysis of the drugs under interest.

Dressing physical parameters such as weight per unit area and fluid handling properties are evaluated. Dressing antiseptic content and release and other chemical parameters such as dressing pH and its stability over the time are analyzed and evaluated. Statistical techniques are used to point out the differences between the products physical and chemical parameters. Different graphs are displayed to compare between the different products in terms of the physical and chemical parameters studied.

Finally it is important to know that the choice of an appropriate antibacterial dressing should be based on the wound type, condition and on clinically applicable measures, such as antibacterial, healing, and exudates handling effects, and not on any single laboratory parameter.

In conclusion, it is suggested to produce surgical dressings impregnated with growth factors and skin substitutes produced form biotechnology, as many types of dressing can then be produced including foam, alginate or hydro fiber matrix. Also, producing more antibacterial dressing impregnated with honey, tea tree oil, clove oil or other natural antibacterial herb extracts in different dressing matrix to combine moisture healing with antibacterial effect of natural products which have less side effects. Finally, Formulation of dressing used after surgical operation which keep the wound moist by balancing its fluid handling capacity together with covering by water proof layer and impregnated with antiseptic and analgesic drugs to comfort the patients after operations.

Conflict of Interest

The authors declare that they don't have any conflict of interest.

REFERENCES

1. Cockbill, S.M., Dressings in Wound Management, Dosage–Drug Delivery Systems, *Encyclopedia of Pharmaceutical Technology*. **2007**, 1023-1037.
2. Russel, A.D., Chlorhexidine: Antibacterial action and bacterial resistance, *Infection*. **1986,** 14, 212-214.
3. Bowler, P.G., Jones, S.A., Walker, M., Parsons, D., Microbicidal properties of a silver-containing hydrofiber dressing against a variety of burn wound pathogens, *J Burn Care Rehabil.* **2004**, 25(2), 192–196.
4. Demling, R.H., DeSanti, L., Effects of silver on wound management, *WOUNDS.* **2001**,13 (1 Suppl A), 5–14.
5. Percival, S.L., Bowler, P.G., Russell, D., Bacterial resistance to silver in wound care, *J Hosp. Infect.* **2005**, 60(1), 1–7.
6. "Test methods for primary wound dressings. Part 1; Aspects of absorbency. Section 3.3- Fluid Handling Capacity (absorbency plus moisture vapour transmission rate, liquid in contact)."*BS EN 13726-1 Section 3.3*, British Standards Institution, **2002.**
7. Guarneri, P., A, Systematic review of silver-releasing dressings in the treatment of burns, *Capsula Eburnea*. **2011**, 6(3), 15-19.

8. British Pharmacopeia **1980**, Chapter: Surgical Dressings. 903-933
9. Parsons, D., Bowler, P.G. Myles, V. and Jones, S., Silver Antimicrobial dressings in wound management: a comparison of antibacterial, physical, and chemical characteristics; *Wounds* **2005**, 17(8), 222–232.
10. Hugo and Russell, Pharmaceutical Microbiology, 7th edition**,** Blackwell Science, Chapter 18**, 2004.**
11. Amorim, C. V., Aun, C. E. nd Mayer, M. P., Susceptibility of some oral microorganisms to chlorhexidine and paramonochlorophenol, *Braz. Oral Res.* **2004**, 18 (3),1806-8324.
12. United States Pharmacopeia 28th ed. National formulary XXIII, *USP28–NF23*, P. 1821, Rockville, Md, **2005.**
13. Hamilton-Miller, J.M., Shah, S. and Smith, C., Silver sulphadiazine: a comprehensive in vitro. Reassessment, *Chemotherapy*. **1993**,39(6), 405-409.