ALGIDEX Ag

SILVER ALGINATE FOAM DRESSINGS

FOR WOUNDS, LESIONS, AND BURNS

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Silver has been known to have an antimicrobial (oligodynamic action) for a considerable period of time. In fact, long before the advent of sulfonamides, during the period of 1939-1942 and before the advent of antibiotics, a USP silver protein known as Argyrol contained from 19 to 25% silver and was utilized for treating cuts and burns and was non-irritating to the skin. There are essentially two different physical states of silver that can be used in the treatment of wounds and burns.

Colloidal silver is metallic silver particles suspended in a base of some other material. The base can consist of water alone or another liquid. Silver particles are metallic silver consisting of clusters of silver atoms. They can range in size from less than a nanometer up to 1000 nanometers (1 micron). Colloidal silver, as are other colloidal particles, are very small particles of silver, so small that they appear to go into solution, but are actually permanent suspensions of insoluble substances. Solutions of colloidal silver will not form visible precipitates of chlorides or proteins unless the colloidal silver is reduced to ionic silver. This important characteristic of colloids is recognized to be exhibited by particles in the size range of about 100 to 10,000 A°. One of the most commonly recognized features of such systems is the fact that particles of a colloid system do not settle out.

Silver ions are silver atoms, which have an electron missing in the outer orbital shell. They are the smallest possible form of silver, about 0.28 nanometers. Silver in the ionic state will precipitate chlorides as insoluble silver chlorides and also precipitate various proteins. Goodman and Gilman (1943) felt that the toxic effect of silver on micro-organisms is due to the silver ions, which precipitate the protein of bacterial protoplasm.

The necessity for metallic silver to be reduced to the silver ionic state prior to its having an oligodynamic action has been supported by innumerable other workers such as Goetz (1943); Rochat and Uzdins (1947); Buonomini and Lapucci (1950); and Liese (1924).

Where a dressing is fabricated entirely of silver, whether the silver is metallic silver in the colloidal form, or is vaporized silver on a cloth, that silver must be reduced to silver ions by one method or another before it will retain a significant antimicrobial activity. Many dressings containing silver in the colloidal form must be moistened with sterile distilled water on a daily basis. Sterile saline cannot be used because the precipitate of silver chloride is highly insoluble in aqueous solutions and would result in very slow release of silver ions.

Alginates, principally calcium alginates have been used in the treatment of wounds and in surgical procedures for many years. Calcium alginate gauze was utilized as a hemostat in neurosurgery by Oliver and Blaine (1950). A patient had suffered meningeal hemorrhage as the result of an automobile accident and had to be operated on to remove a massive blood clot on the dura, following which calcium alginate wool was packed up towards the superior longitudinal sinus from which there was still some hemorrhage. The wound was closed and the alginate wool left *in situ*. The patient's recovery was uneventful, and there were no focal signs of symptoms on discharge 21 days after the operation.

Mullard (1948) reported on 11 cases of extraphleural pneumothorax in which calcium alginate was utilized to control hemorrhage. Mullard reported that the extraphleural space was painted with gauze sponges soaked in 4% sodium alginate followed by repainting with fresh sponges soaked in 2% calcium chloride. The calcium alginate so formed was hemostatic and completely absorbable. They found no unfavorable reactions and no toxic effects were observed in this group of 12 cases.

A recent study by McMullen (1991), reported on the results following the use of calcium alginate non-woven dressing on 11 patients that had a total of 16 wounds of varying severity. She found that the calcium alginate dressings were absorptive without pathology of the healthy surrounding tissue, easy to use, and very comfortable to the patient.

Alginate dressings in knitted and gauze form have been used as hemostats and their successful utilization in surgery reported by Oliver and Blaine. Similar studies and conclusions supporting the hemostatic properties of calcium alginate have been made by Blaine (1951), Joublin (1948), and Hurwitt, *et al.* (1960).

The alginate gauze so used is slowly absorbed when in contact with vascular tissues. Because alginate is a very poor medium for microbial growth, and can readily be softened and removed from the site of application with simple saline solutions or dilute solutions of sodium salts or organic acids, it is particularly useful in extensive wound and burn injuries.

Calcium alginate dressings have been used by Bojrab (1991) in veterinary surgery who reported that the alginate non-woven dressing can be packed onto a capillary bed to stop bleeding and can be left *in situ* because it is completely absorbed.

Soluble silver salts will precipitate alginate from an aqueous soluble solution of sodium alginate to form a compound of silver alginate, hitherto not utilized for the treatment of wounds and burns. The compound of silver alginate combines the desired antimicrobial attributes of the silver ions and the favorable attributes of the alginate moiety. Since all of the silver in the silver alginate foam dressing is in the ionic state, then the availability of ionic silver for the treatment of a wound is immediate and does not require the utilization of sterile distilled water to be placed on a silver dressing every day in order to oxidize the metallic silver colloid to the silver ionic state. The availability of all the silver in the ionic state has also demonstrated that a silver alginate foam dressing will continue to show antimicrobial activity when serially transferred for up to 8 days and even longer so that the dressing need not be changed every day.

It has readily been demonstrated that inoculating the surface of an Algidex Ag silver alginate foam dressing with 10^5 micro-organisms of *Staphylococcus aureus* (ATCC 12600) will show sterility in approximately two hours after inoculation indicating the efficiency of this particular molecular moiety in achieving antimicrobial activity. Further, although many bacteria may differ in the concentration of silver ions necessary to kill them, we had not seen any definitive research that silver resistance occurs in micro-organism exposed to silver ions as occurs with sulfonamides and antibiotics.

However, silver ions may be coupled to a sulfadiazine molecule but microbial resistance to the sulfadiazine, if it occurs, would essentially render those organisms resistant to all other sulfonamides.

The achievement of providing the silver alginate in the state of a microporous foam, which concomitantly prepares a dressing with a built in backing (Algidex Ag™) ensures a very high rate of absorption of exudate from a wound or burn.

The silver alginate with a built-in backing necessarily requires that any exudate from a wound that is absorbed by the silver alginate foam composition, and which exudate may reach the backing whether it consists of cotton, or polyester, or polyurethane foam, would necessarily be free of microbial organisms. Thus the backing applied to a dressing lacking the oligodynamic attributes of the silver alginate could conceivably become the site of microbial multiplication, a possibility that is severely limited if not feasible with the Algidex Ag™.

Where a wound is a result of a laceration that involves the presence of relatively large numbers of micro-organisms, even if the organisms are completely rendered non-viable by the silver ions, there may still result in a marked inflammation and/or hypersensitive reactions at the site of injury due to endotoxins released by the dead microorganisms.

The presence of maltodextrin within the composition of the silver alginate foam dressing acts as a chemotactic agent that attracts leucocytes to the site of inflammation and thereby removes them by phagocytosis (Heggers *et al.*, 1995; Silvetti, A.N., 1981; Silvetti, A.N., 1993; Silvetti, A.N., 1987; Braun, J. *et al.*, 1992; and Schwartz, M., 1987).

Although the silver alginate foam dressings have a superb attribute for absorbing exudate, they can readily be used on dry wounds because they have been fabricated to contain a quantity of bound water and will actually retain a cool feeling to the touch and will not dry out even if exposed to air outside of the packet for many months.

The silver alginate molecules are dispersed in the dressing in a calcium alginate matrix. This particular configuration makes it possible for controlled silver ionic migration to the surface of the dressing in order to react with micro-organisms contained therein. This particular configuration also has the advantage in that the silver alginate-calcium alginate foamed composition can act as a delivery system for such agents as maltodextrin, collagen, or other agents that might be desirable in the treatment of wounds, lesions, and burns.

SUMMATION:

1. Dressings made entirely of metallic silver (Ag°) must contain chemicals to convert the metallic silver (Ag°) to the ionic state (Ag^{+}).
2. Dressings that utilize nitrates to convert Ag° to Ag^{+} may liberate silver nitrate which is toxic to all viable cells.
3. Dressings that contain insoluble silver halides (Cl^{-}, Br^{-}, or F^{-}) must use chemicals to convert the highly insoluble silver salts to soluble ionic silver.

4. Dressings prepared in the form of a silver alginate molecule contain all the silver already in the ionic state.
5. Silver must be in the ionic state to exert anti-microbial activity.
6. There have been no reports of microbial genetic resistance developing to ionic silver when used as an anti-microbial agent.

Silver alginate foam dressings, with or without a backing, and with or without maltodextrin have been approved by the United States Food and Drug Administration.

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