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The Nature and Applications of Tryptic Enzymes in Veterinary Practice

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ENZYMES, or ferments as they were known in earlier times, have been used in medicine for centuries. From the time of Pasteur interest in enzymes has increased till, at the present date, we have active research groups devoting much time and money to the study of the nature and applied uses of a great variety of enzymes. Most chemical reactions which occur in living cells are accelerated by enzymes. Essentially, enzymes are biological catalysts and are protein in nature. Most enzymes are water soluble. As they exist within the mammalian body, enzymes may be surrounded by other proteins. They are thus completely liberated only when this protein is dissolved since they cannot diffuse through it. Enzymes are amphoteric in character and, as such, act as electrolytes in various solutions (1).

Proteolytic enzymes, at the present time, command the greatest interest in the field of medicine and surgery. The common sources of these products are from certain streptococci (streptokinase), the pancreas glands of domestic animals (trypsin), or from the vegetable kingdom as in the case of papain.

Of the three major types papain is perhaps the most proteolytic of the group (1). However, it strongly attacks viable mammalian proteins and is difficult to control unless very closely supervised in its application. For that reason papain has become restricted in routine use in medicine.

The mammalian enzymes such as trypsin and chymotrypsin have been intensely tested as debriding agents in wound treatments and found to be safe for routine use (2, 3, 4, 5). One of the first crude uses of trypsin was in the application of maggots to gangrenous wounds during World War I. It has since been found that the blow fly maggots elaborated a tryptic substance which accomplished an efficient digestion of necrotic material in wounds, especially infected type injuries.

Recent studies (2, 3, 6, 7) in the field of medicine and veterinary medicine have indicated their value in conditions which would require radical surgical procedures to effect debridement of dirty wounds before healing could be accomplished. Trypsin has been used very effectively in the
treatment of topical injuries and has also been successfully used in intrathoracic applications (2, 8) to resolve the empyema associated with tuberculosis.

TRYPSIN AND ITS ACTIONS

Trypsin is available to the veterinary profession in a purified, lyophilized crystalline form (9). This form (Tryptar-Vet®, Armour Veterinary Laboratories) is the activated trypsin and is ready to function, when applied directly to moist wounds or applied by irrigations or wet packs to dry necrotic type lesions. It has been demonstrated both experimentally (2) and clinically (3, 8) that the following sequence of events occur when trypsin is applied to wounds.

The necrotic material can be seen to become loosened and dissolved from the substrate of the wound. Trypsin does not digest normal healthy tissue. Pathological leucocytes rapidly disappear from the wound and normal leucocytes enter into the area. Healthy regenerating tissue forms rapidly to accelerate healing.

There is no side reaction whatsoever attendant with trypsin usage in open, freely-draining wounds. In treating caruncle conditions, as in fistulous withers of the horse, adequate drainage must be established. Tryptic digestion of tissue may liberate histamine substances (6, 8, 10) which could be absorbed and cause a transient pyrexia and occasional stinging. In these instances antihistamine administered at usual dosages for the species will counteract this effect. Upon repeated use of trypsin this phenomenon does not appear again.

The digestive action of trypsin breaks down proteins and partially hydrolyzed proteins at peptide linkages (1, 11). This results in liquefaction of necrotic tissue without formation of intermediate products which may cause anaphylactic reactions. In the human and the animal, trypsin does not cause production of antibodies or any undesirable side reactions when applied topically or in body cavities where aspiration may be accomplished or free drainage established.

It has been demonstrated clinically (3, 6, 7) and most recently in experimental animals that severely infected wounds or cleanly induced surgical wounds (12) treated with trypsin heal more rapidly than similar wounds in control animals. Surgical excision of the nerves controlling the blink reflex of rabbits resulted in regeneration of the nerves on an average of 5 days earlier with trypsin treated animals as opposed to controls. Wound healing which occurs at the skin surface heals on an average of 2 days earlier than controls. Puncture wounds on test animals heal much more rapidly the first 3 days following injury in trypsin treated cases than do untreated controls or controls treated with hydrocortisone.

Trypsin injected parenterally (2, 13, 14, 15) results in a pronounced anti-inflammatory response being elicited in a variety of pathological conditions where inflammation is always present. However, it has been found that intravenous use of trypsin interferes with the anti-clotting mechan-
isms in the blood stream and such action may result in formation of intravascular clots (16,17). This phenomenon will occur in laboratory animals even in the absence of calcium ions. In many case studies (2, 3, 6, 7, 8) trypsin has resulted in the circumvention of radical surgery and has effected permanent healing of many chronic conditions which were refractive to the accepted means of therapy.

This has been adequately demonstrated by Johnson, et al., in the following common conditions. For fistulous withers in horses (cases in which drainage has been established naturally or where surgical incision was required) approximately 400,000 units (Armour units, 1,000 units = 1 mg. trypsic activity) of trypsin daily for 7 days has induced normal repair processes.

A solution of the enzyme may be injected into the area or irrigated through the fistulous tracts. The crystalline material may be blown into the lesions with a powder blower, or it may be inserted in fistulous tracts by use of gelatin capsules.

Foot rot in cattle as with foot canker in horses has been satisfactorily resolved through daily use of trypsin. Two-hundred thousand to 400,000 units applied directly to the lesion or injected into the fistula is sufficient for a daily treatment. Continued for a week or less, this therapy results in normal healing of the condition. This has in several instances circumvented amputation of the claw to correct foot rot.

Trypsin may be injected directly into pus-filled joint capsules, allowed to work for a few hours, then aspirated, leaving the joint free of caseous or purulent material.

In cases of gangrenous and purulent mastitis, depending upon the size of the infected area, 200,000 to 800,000 units of trypsin daily results in considerable reduction of inflammation. The trypsin solution may be introduced into the affected quarter either by way of the teat canal or, if this is impossible, injected with a hypodermic needle directly into the affected area. In the case of gangrenous mastitis, an incision in the area may be required to drain the liquefied material. This therapy must be carried out with indicated antibiotics to control the infection.

It has been found in human cases (8) that the introduction of 500,000 units into the thoracic cavity of chronic tubercular cases with empyema results in a rapid liquefaction of the empyema making possible easy aspiration and drainage of the affected pleura. Also, after a few treatments the tubercular organisms can no longer be detected in the affected area.

Similar effects upon bacteria (2, 3) are noted in many other infected type wounds. Following a few applications of trypsin the invading bacteria cannot be detected. This is assumed to be due to the effect of trypsin upon altering the substrate of the area of injury so that pathogenic bacteria can no longer secure nutrition from the site and, hence, die away. It has also been shown that trypsin digests the capsular material from many pathogenic microorganisms. This must not be construed to mean that trypsin is antibiotic, but this feature combined with such agents enhances the effect of antibiotic therapy in many conditions.

Chronically infected sinuses in cattle and horses have been cured through introduction of trypsin solution into the sinus and allowing it to remain for about 24 hours, then tilting the head or establishing surgical drainage to drain out the liquefied material. This resulted under conditions where antibiotics or methods of flushing the sinus had yielded poor results.

In treatment of topical wounds, abscesses and hematomas, the amount of trypsin to use depends upon the extent and nature of the injury. On the whole, small lesions, a few inches in area, would not require more than 50,000 to 100,000 units of trypsin daily until resolution of the condition is evident. Most of these resolve after one to three applications of trypsin. On more extensive areas, as one might encounter in burns or where much loss of tissue has occurred with acute infection and necrosis, several million units may be required to complete the course of treatment.

Effective dosage will come with experience and usage of the product. As has been indicated previously, one can observe
(over a 30-minute period of time) the rapid digestive action of trypsin upon necrotic tissue. This may serve as an index for future cases and provide a guide for the duration of treatment necessary.

Trypsin must be considered as an adjunct in treatment of dirty, infected and necrotic wounds. Surgical debridement could result in greater loss of body substance and perhaps failure to remove some of the foci of necrosis which may be deeper than is possible to reach. It is easy to see that removal of causes which impede healing and which can be accomplished by enzymatic debridement is often to be preferred to more radical approaches.

**CHYMOTRYPSIN**

Chymotrypsin, an analogue of trypsin, is commercially produced from beef pancreas glands. Its local action upon protein tissue is similar to that of trypsin (1, 18). Chymotrypsin as a purified crystalline material will soon be available to veterinarians for small animal use (Kymar®, Armour Veterinary Laboratories' oil suspension of pure crystalline chymotrypsin). However, the use of this material in human and veterinary medicine is not for topical application.

Chymotrypsin may be safely injected parenterally (intramuscularly) in oil or aqueous suspensions. It does not interfere with the clotting mechanisms of the blood and possesses remarkable anti-inflammatory actions (2, 15, 18, 19, 20, 21). As opposed to many anti-inflammatory products on the market, this enzyme does not have any effect upon the endocrine system of the body. Its mode of action is at present unproved. It does appear to have a selective activity which takes place at sites of inflammation and reduces the edema, pain, and swelling, regardless of cause.

The products may be used prophylactically in preventing inflammatory conditions. This has been effective in preventing inflammation which follows surgical operations such as intestinal surgery, eye surgery, fracture repair, etc. Given prior to such surgical procedures, the edema is held down and rapid healing allowed to take place. At present this product does not appear to be as effective as other anti-inflammatory agents for skin conditions.

Gillispie (22), reporting upon 141 cases of all types in small animals, found that as an anti-inflammatory agent, chymotrypsin was of definite benefit in as many as 75 to 85 per cent of the common conditions for which it was used. The application of the product to the running horse (2) has resulted in dramatic effects upon rate of healing and resolves trauma-induced injuries in a much more rapid period of time than had previously been experienced.

The enzyme may be used prophylactically as well as therapeutically in all conditions in which inflammation and edema retard healing or present a danger to the involved organ. The dosage range which has been employed in small animals is as follows: cats and dogs up to 16 lbs., ¼ cc. intramuscularly every 12 hours; dogs 10 to 50 lbs., ½ cc. every 12 hours; dogs over 50 lbs., ¾ to 1 cc. every 12 hours. In case of severe inflammatory reaction, as in massive trauma, these doses may be given every 8 hours to effect. In large animals doses of 3 to 5 cc. daily result in similar effects.

Some specific conditions in which chymotrypsin is effective in controlling the inflammatory processes and the resultant pain are as follows:

1. Accident or non-surgical trauma as bone fractures, lacerations, contusions.
2. Surgical trauma as mammary tumor excision, perineal hernia correction, open reduction of bone fractures, abdominal surgery.
3. Inflammation of the eye and eyelids as iritis, iridocyclitis, keratitis, conjunctivitis, post-operative panophthalmitis.
5. Cellulitis.
6. Abscesses.

Chymotrypsin hastens the absorption of hematomas, post-operative blood clots in the anterior chamber of the eye and hydropsy.

By reducing inflammation and edema, circulation is restored which in turn hastens absorption and halts tissue necro-
sis with an end result of enhanced healing with a minimum of pain.

The enzyme is non-toxic and has no untoward side effects. It may be used simultaneously with other therapeutic agents without interference.

**SUMMARY**

Purified crystalline trypsin is being widely used in medicine and in veterinary medicine as a substitute for the scalpel in debriding wounds and for the liquefaction of caseous and purulent exudates in abscesses and in body cavities. The enzyme is safe in topical usage and has only occasional mild side effects if excessively used in body cavities.

Trypsin accomplishes effective debridement of wounds and avoids the possibility of greater loss of substance and possible injury to underlying structures which may result from surgical debridement measures. It may also be used in conjunction with surgical procedures to enhance healing in certain difficult cases.

Chymotrypsin, a new enzyme anti-inflammatory agent, is soon to be available to the veterinary profession. It is fully as effective as adrenal steroid type hormones in treating most comparable inflammatory conditions. It possesses the outstanding feature of being absolutely safe from any side reactions in the patient and does not endanger the function or structures of the endocrine system.

Both enzymes are economical to use in routine practice procedures. They are excellent forward steps in relieving the practitioner from more crude or hazardous methods of treating applicable conditions in pets and domestic livestock.

**REFERENCES**


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