Adv Ther (2018) 35:31–42
https://doi.org/10.1007/s12325-017-0648-y

REVIEW

The Role of Trypsin:Chymotrypsin in Tissue Repair

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Received: October 25, 2017 / Published online: December 5, 2017

ABSTRACT

Tissue damage of all types, such as surgical or accidental injuries, fractures, and burns, stimulates a well-orchestrated, physiological process of healing, which ultimately leads to structural and functional restoration of the damaged tissues. The tissue repair process can be broadly divided into four continuous and overlapping phases—hemostasis and coagulation, inflammation, proliferation, and remodeling. If the process is interrupted or halted during any stage, it leads to impaired healing and formation of a chronic wound. Chronic wounds are associated with significant morbidity, mortality, and poor quality of life. Therefore, prompt and effective management of acute tissue injury is necessary to prevent it from progressing to a chronic wound. Proteolytic enzymes have been used to facilitate tissue repair since ancient times. Trypsin:chymotrypsin is an oral proteolytic enzyme preparation which has been in clinical use since the 1960s. It provides better resolution of inflammatory symptoms and promotes speedier recovery of acute tissue injury than several of the other existing enzyme preparations. This review article revisits the role and clinical utility of trypsin:chymotrypsin combination in tissue repair.

Funding: Torrent Pharmaceuticals Limited.

Keywords: Accidental injuries; Burn; Healing; Proteolytic enzymes; Orthopedic injuries; Sciatica; Surgical injuries; Tissue injury; Tissue repair; Trypsin:chymotrypsin

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INTRODUCTION

Impaired tissue repair is a common medical problem, affecting millions of people worldwide [1]. Chronic wounds thus formed are a source of significant morbidity, mortality, and poor quality of life. They also incur substantial healthcare-related financial burden [1–3]. Hence, prompt and effective management of acute tissue injury is necessary to prevent it from progressing to a chronic wound [4].

Proteolytic enzymes have been used to facilitate tissue repair since ancient times. Trypsin:chymotrypsin is an oral proteolytic enzyme preparation which has been in clinical use since the 1960s. It provides better resolution

of inflammatory symptoms and promotes speedier recovery of acute tissue injury than several of the other existing enzyme preparations [4]. This paper revisits the role and clinical utility of trypsin:chymotrypsin combination in tissue repair.

This article is based on previously conducted studies and does not involve any new studies of human or animal subjects performed by any of the authors.

HEALING AND TISSUE REPAIR: INSIGHTS

Tissue damage of all types, such as surgical or accidental injuries, fractures, and burns, stimulates a well-orchestrated, physiological process of healing, which ultimately leads to structural and functional restoration of the damaged tissues. The repair process can be broadly divided into four continuous and overlapping phases—hemostasis and coagulation, inflammation, proliferation, and remodeling [1, 5, 6]. These phases are briefly described below (Fig. 1).

Phase I: Hemostasis and Coagulation

During the phase of hemostasis and coagulation, the damaged blood vessels constrict, platelets get activated, the coagulation cascade is initiated, fibrin clot is formed, and various substances are released from the platelets and damaged cells. These substances cause secondary vasodilation, increase vascular permeability, and act as chemotactic stimuli for different cells which facilitate subsequent repair processes [7]. The provisional fibrin matrix is ultimately invaded and degraded by plasmin—a serine protease which is formed from plasminogen by plasminogen activators, leading to reestablishment of circulation [4, 8].

Phase II: Inflammation

Inflammation starts within 24 h of the injury and lasts for 2 weeks or more. It begins with the release of growth factors and inflammatory cytokines from the activated platelets and the damaged cells, which attract inflammatory cells from circulation—the leukocytes—to the site of injury [9].

Neutrophils are the first leukocytes to reach the injury site where they attach to the vascular endothelial cells and subsequently pass out to the extravascular space [9]. They secrete proteases, including elastase, which degrade and remove cellular debris and hence help in the cleaning up process; α-1 protease inhibitor secreted by macrophages regulates the activity of elastase. Proteases also facilitate migration of neutrophils into the extracellular space where they prevent contamination and infection from local bacterial flora by performing phagocytosis [7, 9, 10]. Additionally, neutrophils release reactive oxygen species (ROSs) which possess anti-infective properties [11, 12]. Also, the proinflammatory cytokines secreted by neutrophils facilitate recruitment of fibroblasts and epithelial cells at the site of injury; these cells are involved in repair and remodeling of the damaged tissue [9].

Blood monocytes begin infiltrating the wound within 2 days of injury [7, 8, 13]. Their entry coincides with decline in neutrophil infiltration. Upon entering the wound, they differentiate into macrophages, which besides participating in phagocytosis of bacteria and muscular debris also perform a very important role of controlling the wound repair process [7, 11]. The latter effect is achieved by numerous cytokines, growth factors, and free radicals secreted by macrophages which regulate recruitment of fibroblasts, endothelial cells, and keratinocytes to the injury site, formation of extracellular matrix (ECM), angiogenesis, and fibrosis [9, 11, 12].

Apoptosis of inflammatory cells, the mechanisms of which remain predominantly unknown, marks the resolution of the inflammatory phase [1, 12].

Phase III: Proliferation

Resolution of the inflammatory phase marks the beginning of the proliferative phase [1]. During this phase, re-epithelialization, angiogenesis, and degradation and remodeling of ECM by proteases (especially matrix metalloproteinases) and their inhibitors occur. This leads to wound closure [5, 11, 12].

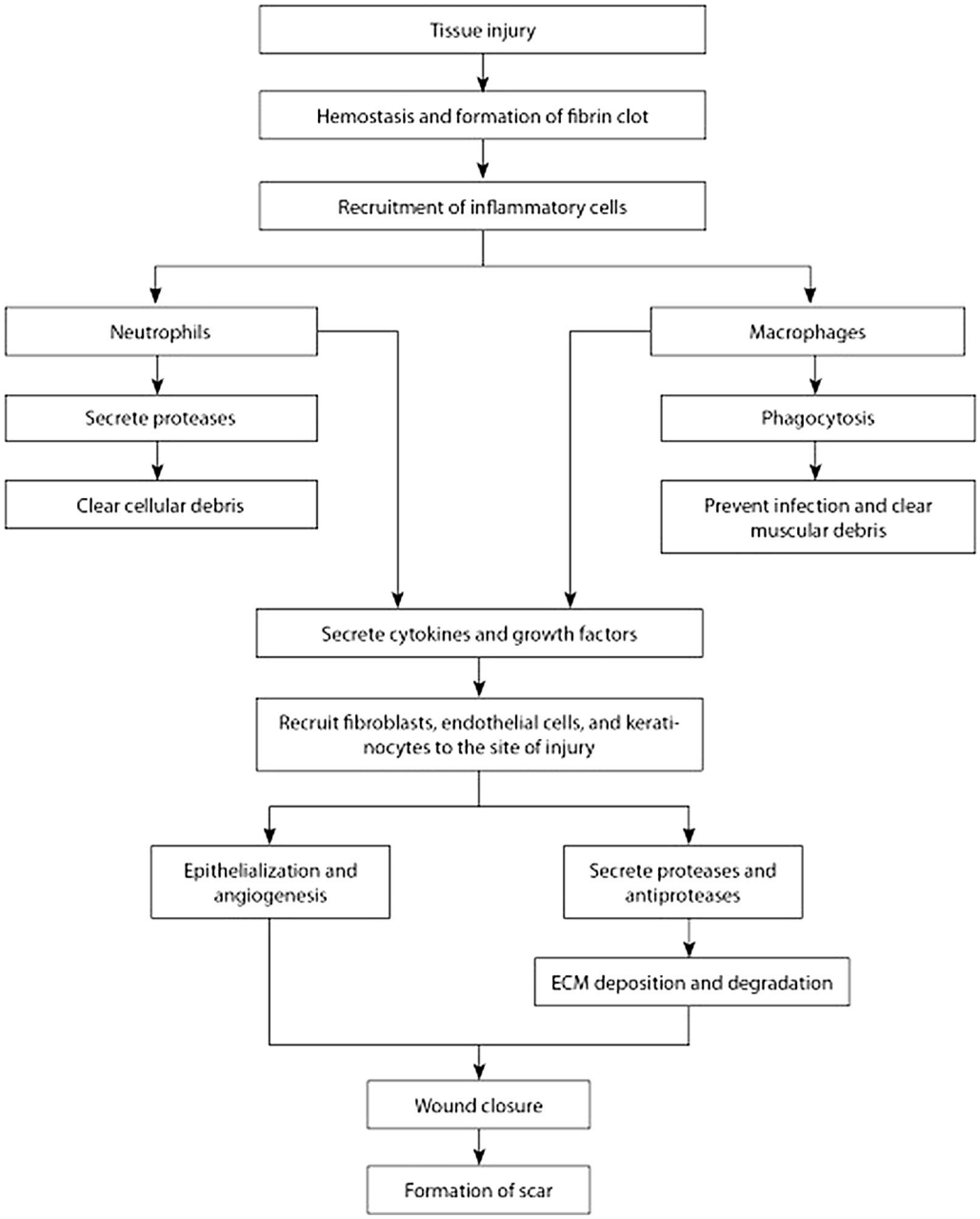

Fig. 1 Normal physiologic process of tissue repair [5, 8–13]

Phase IV: Remodeling

Following wound closure, the remodeling phase begins which leads to formation of a collagenous scar whose tensile strength is approximately 80% of the normal, non-injured tissue [8, 9, 12].

ROLE OF PROTEASES IN TISSUE REPAIR

As discussed in the preceding sections, repair of damaged tissues is a well-coordinated, systematic event which consists of four overlapping yet functionally distinct phases, namely

hemostasis and coagulation, inflammation, proliferation, and remodeling [5, 12]. If the process is interrupted or halted during any stage, it leads to impaired healing and formation of a chronic wound. Usually, chronic wounds are formed as a result of arrest of the repair process during the inflammatory stage [12, 14]. The excessive inflammation thus generated increases the level of proteases relative to their inhibitors. This imbalance disrupts the delicate equilibrium between ECM deposition and degradation that is vital for effective tissue repair, resulting in uncontrolled ECM destruction and formation of a chronic wound [5, 14]. Chronic wounds therefore contain increased levels of inflammatory cells and proteases that do not allow them to heal [12].

Role of Trypsin:Chymotrypsin in Tissue Repair

Trypsin:chymotrypsin is a widely used oral proteolytic enzyme combination to hasten repair of traumatic, surgical, and orthopedic injuries. It shows high bioavailability without losing its biological activities as an anti-inflammatory, anti-edematous, fibrinolytic, antioxidant, and anti-infective agent. These properties help in resolving signs and symptoms of inflammation due to tissue injury and facilitate the repair process. It also demonstrates analgesic effects and reduces the pain associated with healing [4, 15, 16].

Mechanisms of Beneficial Effects of Trypsin:Chymotrypsin in Tissue Repair

Despite extensive evaluation, the mechanisms of beneficial effects associated with trypsin:chymotrypsin combination remain incompletely understood [4]. The postulated mechanisms are briefly discussed below.

Following an acute injury, there is a sharp rise in the levels of the protease inhibitors α1-antitrypsin and α2-macroglobulin. These acute phase reactants inhibit several proteolytic enzymes, which if uncontrolled can lead to unregulated inflammation and impair healing. The order of affinity of α1-antitrypsin with proteolytic enzymes is as follows: elastase > chymotrypsin > cathepsin G > trypsin > plasmin. Similarly, α2-macroglobulin shows greatest affinity with cathepsin G. At this point, it must be reiterated that plasmin causes fibrinolysis and its inhibition prevents fibrinolysis. Therefore, a steep rise in α1-antitrypsin and α2-macroglobulin following acute injury leads to a period of fibrinolytic shutdown, with consequent maintenance of inflammatory response and edema and delay in repair. Oral combination of trypsin:chymotrypsin targets this early stage of inflammation. Since α1-antitrypsin shows greater affinity for trypsin and chymotrypsin compared to plasmin, oral supplementation of the enzyme complex ensures that plasmin remains available for fibrinolysis and the period of fibrinolytic shutdown is shortened. As a result, local microcirculation is restored, inflammatory edema is cleared, and tissue repair is facilitated [4, 17].

Another mechanism which contributes to improved healing with trypsin:chymotrypsin combination is that it helps in maintaining high levels of α1-antitrypsin for a long duration. Consequently, the activity of proteolytic enzymes and their degradative effects are countered, leading to reduction in inflammatory milieu, ROS and oxidative stress, and faster healing. Additionally, the enzyme preparation also increases enzymatic and non-enzymatic antioxidant levels, which further augments its antioxidant and anti-inflammatory efficacy [17–20]. The anti-infective property of the enzyme complex may be explained by enhanced phagocytic activity of natural killer cells and macrophages due to trypsin [4]. It is also interesting to note that the combination has been shown to reduce the constant loss of albumin and pre-albumin after surgical procedures. Consequently, it may prevent many of the life-threatening postoperative complications, such as shock [20]. Overall, the use of trypsin:chymotrypsin in patients with acute injury reduces inflammatory edema and tissue destruction, which in turn facilitates rapid healing [17–19]. Figure 2 provides a comprehensive overview of postulated mechanisms of beneficial effects of trypsin:chymotrypsin in tissue repair [4, 17–20].

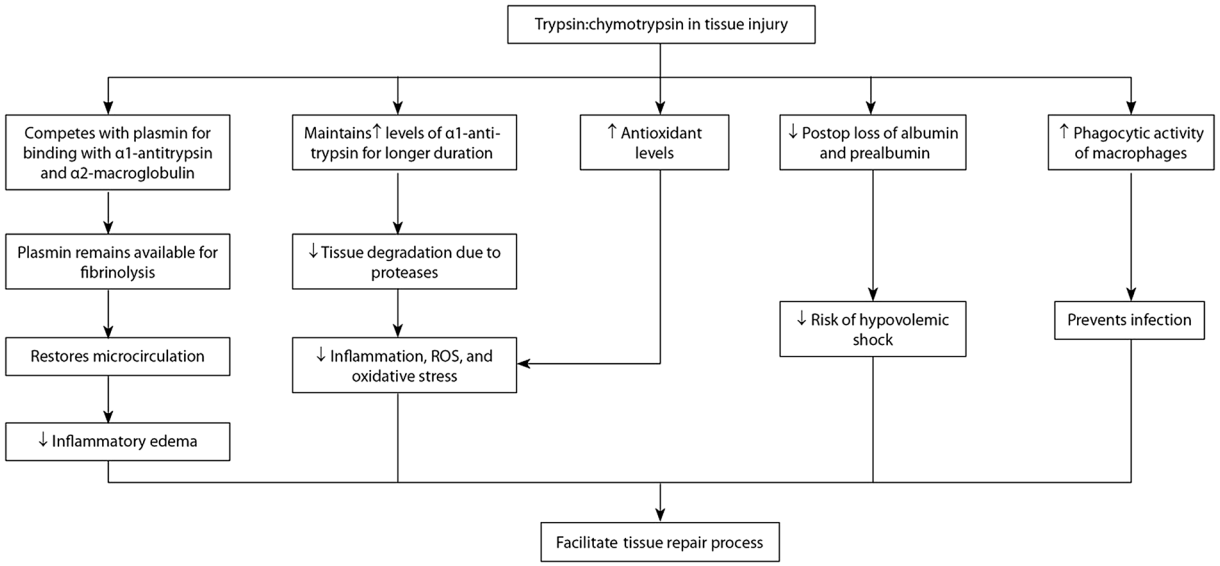

Fig. 2 Mechanisms of beneficial effects of trypsin:chymotrypsin in tissue repair [4, 17–20]

Efficacy and Safety of Trypsin:Chymotrypsin in Various Clinical Indications

Numerous clinical trials have attested the efficacy and safety of trypsin:chymotrypsin combination in resolving inflammation and edema secondary to tissue damage of different types, such as accidental injuries, surgical and orthopedic injuries, burns, and sciatica [4, 15, 21, 22].

Trypsin:Chymotrypsin in Accidental, Surgical, and Orthopedic Injuries—Clinical Appraisal

Goel and Sengupta [15] studied the efficacy of trypsin:chymotrypsin (Chymoral) in accidental soft tissue injuries. They included 156 patients (age between 14 and 45 years) presenting in the casualty department with bruises, lacerations, hematomas, and sprains and strains. The patients were randomized into two groups: the Chymoral group ($n = 79$), which received trypsin:chymotrypsin therapy along with standard emergency treatment, and the control group ($n = 77$), which received emergency treatment only. The recommended dosage of Chymoral was employed, i.e., 2 tablets 4 times a day × 7 days, 30 min before a meal. The patients were followed either once weekly or twice weekly and their progress was documented. Trypsin:chymotrypsin use resolves bruises within 8–12 days, which otherwise cleared in 10–15 days. In patients with lacerations, it improved the appearance of scarring due to stitches. Also, hematomas of the forehead and knees, which usually take 2–3 weeks to clear, resolved within 10–12 days in the Chymoral group. Ankle sprains normally take 2–3 weeks to recover. However, speedy recovery was documented with trypsin:chymotrypsin use, clearing as quickly as within 7–12 days. Additional benefits associated with the use of the enzyme preparation included relief in pain and lower incidence of infection. It was concluded that trypsin:chymotrypsin treatment in patients with accidental soft tissue injuries hastens the healing process and significantly reduces the recovery time. Table 1 shows major findings of the study.

Further validating the above findings, Brakenbury and Kotowski [21] also demonstrated that trypsin:chymotrypsin treatment improved the recovery rate in patients with ankle sprains. They conducted a double-blind randomized controlled trial involving 252 patients with sprains of the medial/lateral ligaments of the ankle that were immobilized using either below-the-knee plaster cast or an elastic bandage applied from the toes to below the knee. The patients were randomized to receive either

Table 1 Comparative recovery time with and without trypsin:chymotrypsin (Chymoral) in patients with accidental soft tissue injuries [15]

Type of injuries	Chymoral (trypsin:chymotrypsin) group		Control group	
	No. of cases	Recovery time	No. of cases	Recovery time
Painful bruises				
Facial and forehead bruises	6	8–12 days	6	10–15 days
Facial bruises and injury to nose	10	8 days	10	15 days
Facial bruises and black eyes	2	10–12 days	2	20 days
Soft tissue crush injury of thigh, with arm bruises and toe wounds	2	12 days	2	4 weeks
Hematomas				
Forehead hematoma, without skull fracture	10	10 days	10	15–20 days
Knee hematoma	5	12 days	5	3 weeks
Ankle sprain with bruises but without fracture				
Lateral side bruises	20	10–12 days	20	2–3 weeks
Medial side bruises	10	8–10 days	12	2–3 weeks
Foot bruises	4	10–12 days	0	–

$p \leq 0.02$

trypsin:chymotrypsin (Chymoral Forte) or placebo. Chymoral Forte contains 100,000 Armour units of proteolytic activity and was given half an hour before meal, 4 times a day × 5 days. In total, four groups were formed: group 1, trypsin:chymotrypsin and plaster cast; group 2, placebo and plaster cast; group 3, trypsin:chymotrypsin and elastic bandage; and group 4, placebo and elastic bandage. The patients were examined and evaluated for bruising and edema, power of dorsiflexion, and range of movement at baseline and at day 7 and day 14. The extent of bruising and edema was assessed on a scale of 0–3 as absent, mild, moderate, and severe. A hand-held Hammersmith myometer was used to measure power of dorsiflexion and range of movement was recorded by goniometer. The following results were noteworthy:

- Among patients with a plaster cast, the rate of resolution of bruising was better in those who received trypsin:chymotrypsin treatment than in placebo on both day 7 and day 14 (Fig. 3a).
- Among placebo group patients, the use of an elastic bandage produced faster resolution of bruising and edema than plaster cast on both day 7 and day 14.
- Improvement in power of dorsiflexion was fastest in those treated with an elastic bandage and trypsin:chymotrypsin.
- The complete global response rate at day 14 was better in those who received trypsin:chymotrypsin treatment than placebo (Fig. 3b).

These findings suggest that trypsin:chymotrypsin treatment hastens the recovery of accidental soft tissue injuries.

Besides accidental injuries, the reparative role of trypsin:chymotrypsin has also been appreciated in surgical injuries. A multicentric Indian study [17] investigated the efficacy and safety of trypsin:chymotrypsin (Chymoral Forte) in patients with traumatic injuries from accidents, surgeries, burns, and others. A total of 230 patients were recruited from 28 districts across India; 208 patients completed the study and the remaining were lost to follow-up. These

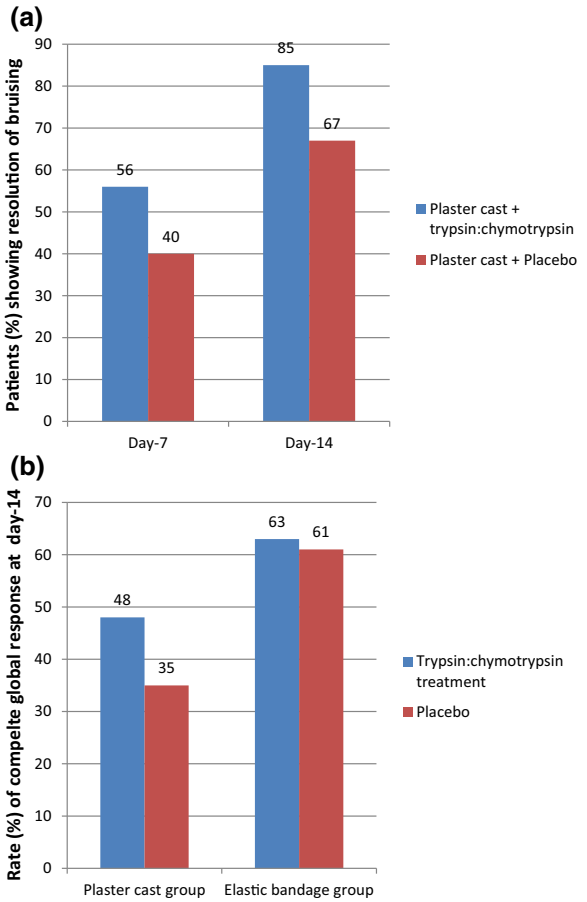

Fig. 3 **a** Resolution of bruising with trypsin:chymotrypsin treatment vs placebo in patients with ankle sprain who had a plaster cast [21]. **b** Global response at day 14 with trypsin:chymotrypsin treatment vs placebo in patients with ankle sprain who had either a plaster cast or elastic bandage [21]

patients received 1 tablet of Chymoral Forte 4 times a day × 5–10 days. The levels of swelling, pain, and inflammation were measured on day 0, 2, 4, 6, 8, and 10. Also, improvement in hematoma, healing of wound, and mobility was evaluated. At the end of the study, the overall efficacy of the treatment was measured on a 3-point scale as excellent (no signs and symptoms of inflammation), good (swelling reduced, and no pain or other symptoms), and fair (some degree of pain, swelling, and other symptoms). Statistically significant improvement in pain, swelling, and inflammation was noted from the 6th day onwards; $p < 0.05$ (Table 2). Likewise, improvement in hematoma, healing of wound, and mobility was noted by 6th day, which

Table 2 Improvement in swelling, pain, and inflammation with trypsin:chymotrypsin (Chymoral Forte) treatment in patients with traumatic injuries [17]

	Mean swelling score ($p < 0.05$)	Mean pain score ($p < 0.05$)	Mean inflammation score ($p < 0.05$)
Baseline	2.46 ± 0.8	2.46 ± 0.8	2.29 ± 0.86
Day 6	0.99 ± 0.76	0.74 ± 0.71	0.81 ± 0.7
Day 8	0.51 ± 0.62	0.38 ± 0.56	0.41 ± 0.55
Day 10	0.22 ± 0.46	0.16 ± 0.41	0.1 ± 0.32

further increased significantly by 10th day; $p < 0.05$. At the end of the study, the overall efficacy of the treatment was determined to be excellent in 48.2% patients, good in 44.7% patients, and fair in 7.0% patients (Fig. 4). No case of therapy discontinuation due to drug-related adverse events attested the acceptable tolerability of trypsin:chymotrypsin. On the basis of these findings, it was suggested that trypsin:chymotrypsin treatment in patients with surgical injuries, accidental injuries, and burns effectively resolves inflammation and improves healing.

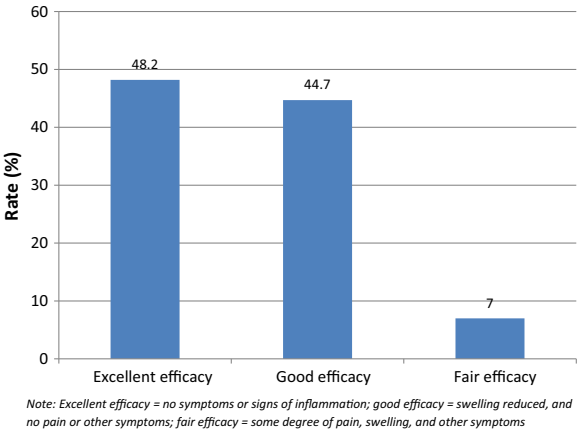

Fig. 4 Overall efficacy of trypsin:chymotrypsin (Chymoral Forte) treatment in resolving signs of inflammation in patients with traumatic injuries [17]

Usefulness of trypsin:chymotrypsin treatment has also been recognized in orthopedic injuries and surgeries. Pages [23] conducted a clinical trial to investigate efficacy, safety and tolerability of trypsin:chymotrypsin (Chymoral Mauchant) treatment to resolve edema and hemorrhagic infiltration due to tissue trauma in orthopedic surgery patients. Chymoral Mauchant contains 50,000 Armour units of trypsin and chymotrypsin, and in an adult of average body weight, 6–8 tablets daily were given. Good and rapid absorption of edema and hemorrhagic infiltration was interpreted as an "excellent result" and good but delayed resolution of edema as a "good result" [23]. In 15 adult patients who were treated therapeutically with trypsin:chymotrypsin for the indications of maxillofacial injury, fractures, knee sprain, traumatic hematoma of the leg and thighs, hemarthrosis of the knee, and burns, excellent results were produced in 46.67% patients, good results in 40% patients, average results in 6.67% patients, and no improvement in 6.67% patients. Its prophylactic use in 15 adult patients for the indications of meniscectomy, fractures, skin grafting, digit amputation, repair of nerves and tendons, and repair of unsightly harelip open scar yielded excellent results in 86.67% patients, good results in 6.67% patients, and average results in 6.67% patients. The observation that none of the patients reported any side effects established its good safety and tolerability profile. It was concluded that in orthopedic surgery patients, therapeutic use of trypsin:chymotrypsin reduces edema and hemorrhagic infiltration. Furthermore, it can be used prophylactically as well to prevent edema and hematoma formation and reduce postoperative complications.

Further direct evidence of the valuable role of trypsin:chymotrypsin in orthopedic settings can be gleaned from another study [4], which demonstrated its use to promote healing in patients with orthopedic surgical injuries. This randomized controlled study involved a total of 75 patients who had undergone open reduction of fractures. These patients were randomized to receive trypsin:chymotrypsin (Chymoral Forte), serratiopeptidase (S) 5 mg oral tablets, or an oral enzyme combination of trypsin 48 mg, bromelain 90 mg, and rutoside 100 mg (TBR). The medications were started 24 h after the surgery, 3 times a day for 7–10 days. Improvement in erythema, local irritation, wound discharge, edema, induration, tenderness, and pain were documented on follow-up visits on days 3, 5, 7 and if required on day 10. Global response was assessed at the end of the therapy (day 7 or day 10) using the 5-point Patient Global Assessment of Response to Therapy (PGART) scale; 1 = excellent response, 2 = good response, 3 = average response, 4 = no response, 5 = poor response. Similarly, tolerability of treatment was assessed at the end of the therapy using the 5-point Patient Global Assessment of Tolerability to Therapy (PGATT) scale; 1 = excellent tolerability, 2 = good tolerability, 3 = average tolerability, 4 = poor tolerability, 5 = very poor tolerability. Trypsin:chymotrypsin treatment produced significantly greater improvement in erythema, local irritation, wound discharge, edema, induration, tenderness, and pain than serratiopeptidase and trypsin:bromelain:rutoside treatments. The overall efficacy and tolerability of trypsin:chymotrypsin was also significantly superior to other treatments (Figs. 5, 6).

It was concluded that trypsin:chymotrypsin treatment is significantly better tolerated and more effective than other enzyme preparations in resolving symptoms of inflammation after orthopedic surgeries and therefore promotes better healing [4].

Trypsin:Chymotrypsin in Burn Injuries—Clinical Appraisal

Burn injuries are the most severe injuries sustained by the human body [6]. The phases of healing are similar to those that occur in any other type of tissue injury. However, in contrast to other traumatic injuries, burn injuries cause generalized increase in vascular permeability, which leads to localized and generalized edema and hypovolemic shock [24]. Shock, in turn, is associated with enhanced generation of free radicals, which cause lipid peroxidation and subsequent further damage to tissues and organs [19].

Trypsin:chymotrypsin treatment in patients with burn injuries reduces edema,

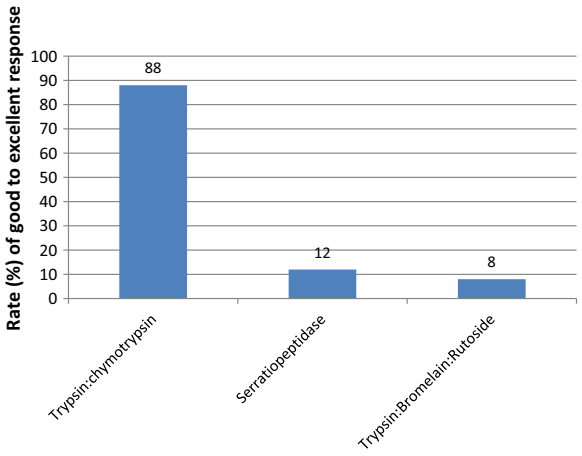

Fig. 5 Patient Global Assessment of Response to Therapy (PGART) for efficacy in patients with orthopedic surgical injuries who received either trypsin:chymotrypsin (Chymoral Forte), serratiopeptidase, or trypsin:bromelain:rutoside [4]

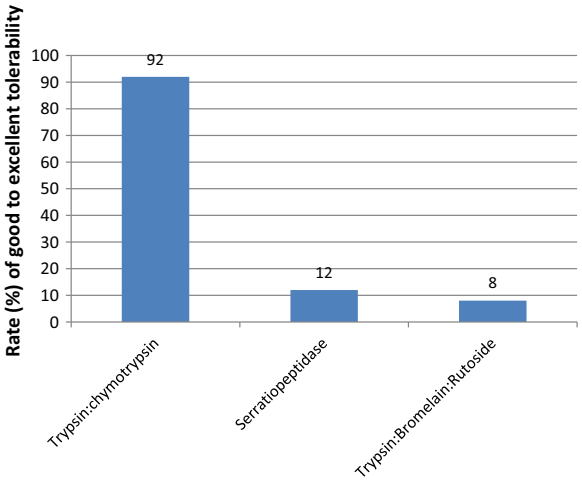

Fig. 6 Patient Global Assessment of Tolerability to Therapy (PGATT) for tolerability in patients with orthopedic surgical injuries who received either trypsin:chymotrypsin (Chymoral Forte), serratiopeptidase, or trypsin:bromelain:rutoside [4]

inflammation, and oxidative stress which in turn attenuates tissue destruction and hastens the repair process [6, 19].

Latha et al. [6] investigated the effects of trypsin:chymotrypsin treatment on acute phase proteins [C-reactive protein (CRP), α1-antitrypsin, and α2-macroglobulin] in 30 patients with 20–30% deep second-degree burns. These patients were grouped into two groups: the enzyme-treated group, which received trypsin:chymotrypsin (Chymoral Forte DS having enzymatic activity of 200,000 Armour units) 4 times a day for 10 days, and the control group, which did not receive the enzyme treatment. An initial increase in the levels of acute phase proteins(CRP, α1-antitrypsin, and α2-microglobulin) was recorded in both groups. The anti-inflammatory efficacy of trypsin:chymotrypsin was reflected by a decline in CRP levels by day 7 in the enzyme-treated group, which otherwise remained high in the control group; note: CRP is an indicator of inflammation. Other notable findings were significant differences in the levels of α1-antitrypsin and α2-macroglobulin between the two groups. While α1-antitrypsin levels started gradually declining from the 3rd day onwards in the control group, in the enzyme-treated group they continued to rise, reaching a maximum on the 5th day, and thereafter remained at the higher levels for a longer duration. Trypsin inhibitory capacity (TIC) was consequently higher in the treated group than the control group. The increase in α2-macroglobulin levels was also greater in the treated group than the control group. It was suggested that apart from its anti-inflammatory, anti-edematous, and fibrinolytic actions in burn injuries, the enzyme complex minimizes protease-induced tissue degradation by maintaining higher levels of proteolytic inhibitors (α1-antitrypsin and α2-macroglobulin) for longer durations. Thus, it facilitates healing of burn injuries by reducing inflammation, edema, and tissue destruction.

The investigators of the aforementioned study also evaluated the antioxidant efficacy of trypsin:chymotrypsin in the same cohort of burn patients. The lipid peroxidation products, which increased initially in both the treated and the control groups, started to decrease in the treated group from the 7th day onwards. Also, enzymatic and non-enzymatic antioxidant levels were higher in the treated group than the control group and remained at high levels for longer durations. These findings support the aforementioned observations that trypsin:chymotrypsin reduces tissue degradation, which in turn leads to decreased formation of free

radicals and hence maintenance of higher antioxidant levels for longer durations [19].

Trypsin:Chymotrypsin in Sciatica—Clinical Appraisal

Sciatica is a painful condition characterized by pain radiating from the lower back to the leg. In the majority of cases, it is caused by intervertebral disc herniation, resulting in spinal nerve root compression and inflammation [25]. The anti-inflammatory efficacy of trypsin:chymotrypsin could therefore be utilized in these patients to reduce inflammation and improve symptoms [22].

Gaspardy et al. [22] evaluated the effectiveness of trypsin:chymotrypsin (Chymoral tablets) treatment to improve symptoms of sciatica due to intervertebral disc herniation. They conducted a double-blind cross-over trial involving 30 patients (age between 23 and 70 years) with sciatica, who had previously failed analgesics, physiotherapy, and injections of local anesthetics. The participants were randomly assigned into two groups. Group 1 first received trypsin:chymotrypsin treatment and subsequently placebo treatment, and group 2 first received placebo treatment and subsequently trypsin:chymotrypsin treatment. The dosage of trypsin:chymotrypsin and placebo was 2 tablets 4 times a day for 3 days followed by 1 tablet 4 times a day for 4 days. In addition to the study treatments, all patients received bed rest, electrotherapy, analgesics, etc. Patients' condition was assessed at baseline and at 7-day intervals. Symptom severity was graded on a scale of 0–4 and straight leg raising test was measured in degrees. At 1 week, group 1 patients who first received trypsin:chymotrypsin treatment showed considerable decrease in symptoms compared with group 2 patients who first received placebo. At 2 weeks, group 1 patients did not document any further decrease in symptoms, whereas group 2 patients witnessed a marked reduction in symptoms (Table 3).

It was suggested that trypsin:chymotrypsin treatment in patients with sciatica secondary to intervertebral disc protrusion significantly improves symptoms by decreasing inflammatory edema in the nerve roots [22].

Table 3 Impact of trypsin:chymotrypsin treatment on sciatica symptoms [22]

Symptoms	Rate (%) of improvement in group 1		Rate (%) of improvement in group 2	
	Week 1 (trypsin:chymotrypsin treatment)	Week 2 (placebo treatment)	Week 1 (placebo treatment)	Week 2 (trypsin:chymotrypsin treatment)
Spontaneous low back pain	60	60	20	53.3
Spontaneous leg pain	46.7	46.7	33.3	46.7
Lumbar muscle spasm	54.5	72.7	33.3	53.3
Lumbar rigidity	73.3	73.3	33.3	60.0
Scoliosis	62.5	62.5	30.0	70.0
Sensitivity to pressure in paravertebral region	53.3	53.3	6.7	80.0
Straight leg raise test	53.3	53.5	13.3	53.3

CONCLUSIONS

Owing to anti-inflammatory, anti-edematous, fibrinolytic, anti-infective, and analgesic effects, trypsin:chymotrypsin oral combination has emerged as a promising treatment to facilitate healing of traumatic injuries. It promotes speedier recovery and better resolution of inflammatory signs and symptoms due to tissue injury than several of the other existing enzyme preparations. It also demonstrates analgesic effects and reduces pain associated with healing. The efficacy and safety of trypsin:chymotrypsin in accidental injuries, surgical and orthopedic injuries, burns, and sciatica has been corroborated by a substantial and largely consistent body of evidence from clinical trials.

ACKNOWLEDGEMENTS

Funding. Article publication charges were funded by Torrent Pharmaceuticals Limited.

Authorship. All named authors meet the International Committee of Medical Journal Editors (ICMJE) criteria for authorship of this manuscript, take responsibility for the integrity of the work as a whole, and have given final approval for the version to be published.

Medical Writing, Editorial, and Other Assistance. The medical writing support has been provided by Springer India Pvt Ltd and was funded by Torrent Pharmaceuticals Ltd.

Contributorship. The authors would also like to acknowledge Ms. Surbhi Sarvaiya for her contribution towards the execution of this project.

Disclosures. Dilip Shah and Kushal Mital have nothing to disclose.

Compliance with Ethics Guidelines. This article is based on previously conducted studies and does not involve any new studies of human or animal subjects performed by any of the authors.

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