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A REVIEW: OVERVIEW ON SERRATIOPEPTIDASE - THE MIRACLE ENZYME

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ABSTRACT

Serratiopeptidase it is a proteolytic enzyme that degrade peptide bond in protein. It was isolated from the intestine of silk worm. Its name derived from its origin. The isolated Serratia marcescens from soil, water surface or any moisture rich environment. It is extracellular enzyme. enzyme activity check by zone observed around colony by utilization of gelatine, skim milk, casein. Production of enzyme using trypticase soy broth at optimum temperature 32℃, optimum pH 7.3, maximum production within 25 hours. The chemical and UV mutated strain produce a higher amount of enzyme production than wild type strain. The enzyme purified by ammonium sulphate precipitation method, HPLC, dialysis, DEAE cellulose column chromatography, gel filtration etc. The enzyme activity inhibited by tween 20, EDTA, organic acid or metal ion. It is very use full in therapeutically in various disease like UTI, endocarditis, chronic lung infection, osteomyelitis, chronic sinusitis, migraine is, fibrocystic breast disease, asthma, ovarian cysts etc.

Keywords*: - Serratiopeptidase, production, purification, optimization, purification, Serratia marcescens*

1. INTRODUCTION

Enzyme are protein in nature which is responsible for all chemical reactions. It is act as biocatalyst that is increase the rate of reaction (Cech T R, Bass B L., 1986) serratiopeptidase also called a serrapeptase, serratiapeptase, serralysin, Serratia peptidase (Gowri Sivaramakrishnan and Kannan Sridharan, 2018) Serrapeptase is a protease extracellular enzyme that is produce by a Serratia marcescens. Enzyme contain a 3 molecule of zinc ligand which is responsible for catalytic activity (Hamada K. et. al, 1996). Serrapeptase is bind to α 2 macroglobulin in equal ratio in blood that is act as a anti-inflammatory reaction (Khateeb T.H, Nuair Y. ,2008). Serrapeptase (STP) is very useful in therapeutically. it is reducing the pain, anti-oedemic, analgesic, it is act as fibrinolytic that is dissolve a blood clot (Klein G, Kullich W., 2000). Chemical structure of serrapeptase does not bind to protein in healthy tissue so it cannot affect healthy tissue (Robert S R ,2009). Serrapeptase isolated from the different strain of serratia - Serratia marcescens. serratia indica, serratia plymuthica and strain E -15; Bacillus licheniformis; Streptomyces hydrogenans but the Serratia marcescens strain E-15 that produce a highest amount of enzyme this strain is isolate from the intestine of the silk worm (S. Moore and W. H. Stein,1963), (T. W. Goodwin and R. A. Morton, 1946), (J. R. Spies and D. C. Chambers ,1949), (P. E. Wilcox ,1967). Serrapeptase is also called a “miracle enzyme” because its wide range application on human body (Atlas, R. M., 1993).

2. PRODUCTION OF SERRATIOPEPTIDASE ENZYME FROM SERRATIA MARCESCENS

The Serratia marcescens commonly found in different soil sample it is normally present in the moisture rich environment it also presents in the water surface, toilet bowl, bathtub, shower stall, digestive track of mammals.

Table 1. Sources of serratiopeptidase:

Sr. No.	Name of bacteria	Strain	Source	Reference
1	*Serratia marcescens*	E 15	Intestine of silk worm	Anil et al., 2013

2	*Serratia marcescens*	VITSD2	Soil	Robert et al., 2009
3	*Serratia marcescens*	NRRL B-23112	Soil	Salamone et al., 1997
4	*Serratia sp.*	ZF03	Hot springs	Salarizadeh et al., 2014
5	Serratia marcescens	NCIM 2919	Not mention	Wagdarikar et al., 2015
6	*Bacillus licheniformis*	NCIM 2042	Not mentioned	Wagdarikar et al., 2015
7	*Serratia marcescens*	SRM	Flowers of summer squash	Kaviyarasi et al., 2016
8	*Streptomyces hydrogenans*	Not mentioned	Mangrove soil	Nageswara et al., 2016
9	*Streptomyces hydrogenans*	MGS1	Soil	Vanama et al., 2014
10	*Serratia marcescens*	P3	Soil	Bach et al., 2012
11	*Actinomycetes*	kMFGS13	Mangrove soil	Jyothi vanam, *et. al*,2014
12	*Serratia marcescens*	S6	Soil	Ahmed Ammar, *et. al,* 2019)
13	*Serratia spp.*	DT3	Soil	Nguyen, T. T. and Quyen, D. T., 2011
14	*Serratia marcescens*	KU296189.1	Marine water	Anusha Krishnamurthy, *et. al,* 2015

15	*Serratia spp.*	RSPB11	Marine habitat	Lakshmi Bhargavi,*et.al*, 2012
16	*Serratia marcescens*	AD-W2	Soil	Devtulya Chander, *et. al*, 2021

Serratia marcescens hydrolyse the casein agar (Mohankumar A, Raj RHK,2011),skim milk agar (Romero FJ, et.al,2001), .gelatine agaragar (Nakamura S, et. al, 2003) for production of serratiopeptidase enzyme and produce extracellularly observe zone around colony isolated Serratia marcescens strain for production of serratiopeptidase enzyme in different medium such as tryptone soya broth (Sambrook, J. a. D. R., 2001) tryptone yeast extract broth (Kreger, A. S. and Gray, L. D., 1978) nutrient broth glucose culture medium (Longo, M. A., et.al,1999) , starch casein broth medium (Doddapaneni, K. K.et.al,2009) casein yeast extract medium (Najafi, M. F,et. al, 2005) trypticase soy broth use for optimum production of enzyme (Devi C S, et. al, 2013) Strains delivering Serrapeptase particularly Serratia marcescens are generally refined in trypticase soy stock. A medium containing carbon source-maltose, natural nitrogen source-peptone, inorganic nitrogen source-ammonium sulfate, dihydrogen phosphate, sodium bicarbonate, inorganic salt source-sodium acetic acid derivation, glycerin and ascorbic corrosive can be utilized as a creation medium and this medium yielded about 27.36 U/m (Badhe R V, et. al, 2009). Another medium revealed for creation of Serrapeptase contained maltose 45 g/l soybean feast 65 g/l, KH2PO4 8.0 g/l, and NaCl 5.0 g/l at a pH 7.0 which gave a greatest yield of 32575EU/mg. (Pansuriya R C, Singhal R S., 2010) A mix of tryptic soy stock (30 g/l) and skim milk (5% w/v) (TSB-SM) medium can likewise be utilized which is equivalent to Serrapeptase creation involving glucose insignificant mechanism for 48 h with ensuing expansion of 10% (w/v) skim milk at incubation time is 12 h (Salamone P R, Wodzinski R J, 1997) Feather meal stock can additionally be utilized for enzyme creation that contains feather Meal, sodium chloride, KH2PO4 and K2HPO4(Bach E,et.al,2012). Partial purification of enzyme by ammonium sulfate precipitation, dialysis, ultra-filtration, watery two-stage frameworks, High-Performance Liquid Chromatography (HPLC) and so on (Bach E,et.al,2012), (Devi C S,et.al,2013). Serrapeptase can likewise be purified by ultrasound helped three stage dividing technique, which just concentrate it. This technique has a few benefits like single step process, simple scale-up, represents around 96% recuperation of Serrapeptase with a 9.4-overlay level of purification in 5 min of cycle time under ideal circumstances (Pakhale S V, Bhagwat S, 2016).

Maximum production of enzyme can be observed in 32℃ to 37℃ (Anil C S, Kashinath M A, 2013) and optimum incubation period (24 hours). The stability of enzyme up to 42℃ at 45℃ its loss activity up to 25%. At above 55℃ to 60 ° C enzyme will be denatured (Salarizadeh N, et. al, 2014)The enzyme will be stable up to pH 7.3 (Anil C S, Kashinath M A, 2013) the most suitable carbon source for Serratia marcescens is glucose and nitrogen source are tryptone for high production of serratiopeptidase enzyme (Wagdarikar J M, et.al,2015). The effect of UV light on Serratia marcescens it will increase the enzyme activity the S. marcescens expose in UV light up to 20 second the 1575.3 EU/ml of enzyme activity are Observe (Ayswarya A,et.al,2013)The enzyme can be purified by ammonium sulphate precipitation, dialysis, acetone fractionation, gel filtration, HPLC etc. (Kouichi Miyata, et.al, 1970). The molecular weight of serratiopeptidase can be determine by the SDS - polyacrylamide gel electrophoresis. It having 5% stacking gel and 12% separating gel and 50,000 KDa can determine (Longo, M. A, et. al, 1999) Serratiopeptidase enzyme also produce by a Bacillus licheniformis and it will produce 22.85 IU/ml using appropriate medium (Wagdarikar J M, et.al,2015). Streptomyces hydrogenans also produce enzyme by using low-cost substrate horse gram under solid state fermentation (Nageswara S,et.al, 2016).

3. OPTIMIZATION OF DIFFERENT PARAMETER:

3.1. Effect of temperature:

Serratia marcescens produces the most Serrapeptase at temperatures between 32℃ (Mohankumar A, Raj RHK., 2011) to 37℃ (Anil C S, Kashinath M A, 2013). Hence The optimal temperature range for Serratiopeptidase production is 32℃ to 37℃. Serrapeptase production at its peak. Temperatures of 0°c or less Above this range, the yield was decreased (Anil C S, Kashinath M A, 2013). The optimal temperature for maximal Serrapeptase production by *Bacillus licheniformis* produces at a temperature of around 35℃.(Wagdarikar J M,*et.al*,2015) Serrapeptase is stable at temperatures up to 42℃. Above 42℃, the enzyme's activity rapidly diminishes or due to high temperature the enzyme is denatured (Salamone P R, Wodzinski R J., 1997) Serrapeptase is working at its best. It was active in the 50℃-55℃ range, and at 45℃, it retained 85 percent of its activity. At 60℃, it lost a quarter of its enzyme activity and fell to 25%.(Salarizadeh N,*et.al*,2014). It was discovered that when *Serratia marcescens* was exposed to varied temperatures of 28℃, 32℃, 37℃, and 40℃, enzyme activity increased. maintained until a maximum temperature of 32℃ is reached (Manal K M.,2015). Metalloprotease from *Serratia spp.* ZF03 give a optimal production at 50° to 55°C temperature (Salarizadeh N,*et.al*,2014).

Protease protein created by *Serratia marcescens* - S6 was dynamic and stable at temperature going from 20 to 50 ^{0}C for 120 min, then, at that point, its solidness and action diminished by expanding the brooding temperature. What's more, solidness of protease protein was marginally diminished at temperature going from 50 to 80 ^{0}C, giving exercises going from 397 to 324 U/mm (Ahmed Ammar,*et.al*,2019). At 32° C temperature produce a maximum enzyme and give a highest clearing zone on skim milk agar the 36 mm in size by *serratia marcescens* (Mohankumar A, Raj RHK., 2011).

3.2 Effect of pH:

The optimal pH for maximum Serrapeptase production from Serratia marcescens is 5.0 to 9.0, with phosphate buffer being the best buffer, while a noticeable fall in productivity can be noticed at pH 9.0. pH values that are both higher and lower than the ideal pH that reduce enzyme (Mohankumar A, Raj RHK.,2011). The enzyme works even at pH 9.0. It is stable in its active form (Salarizadeh N,et.al,2014). According to another study, the ideal pH for best performance is 7.2. Serratia marcescens produced serrapeptase (Anil C S, Kashinath M A., 2013). pH ideal for optimum results by Bacillus licheniformis produced at 6.5 pH serrapeptase (Wagdarikar J M, et.al,2015). Optimal pH to get the most out of your plants Streptomyces hydrophilus serrapeptase production of 85 U/gds from Streptomyces hydrogenans ranged from 6.5 to 7.0 (Nageswara S,et.al,2016). The enzyme produces by serratia marcescens at pH 7.3 it gives a maximum size of zone 3.2 mm on skim milk agar (Manal Khalid, 2016).

3.3 Effect of incubation period:

In order to determine the production and activity of any enzyme, the incubation time is crucial. Serrapeptase generation from Serratia marcescens requires a 24-hour incubation period (Mohankumar A, Raj RHK., 2011) to a 25-hour incubation period (Anil C S, Kashinath M A., 2013). The best time to incubate Bacillus Licheniformis for maximum Serrapeptase synthesis is 24 hours (Wagdarikar J M, et.al,2015). At 25 hours of incubation, it gives a maximum zone 3.4mm on skim milk agar plate (Manal Khalid, 2016).

3.4 Effect of different media composition:

When both tryptone and yeast extract are added to the solution in the absence of glucose, maximum Serrapeptase synthesis can be achieved (Anil C S, Kashinath M A., 2013). Glucose is the most abundant carbon source for Serratia marcescens, while Glycerin and Maltose are the most abundant carbon sources for Bacillus licheniformis. Tryptone is the greatest nitrogen source for Serratia marcescens and Bacillus licheniformis. Serrapeptase concentration rose from 16.52 IU/ml to 22.85 IU/ml after media optimization for Bacillus licheniformis (Wagdarikar J M, et.al,2015). To increase Serrapeptase yield by Streptomyces hydrogenans MGS13, a surface response approach of media components was examined. The response surface approach is an empirical statistical modelling tool for solving multi-variable equations simultaneously in multiple regression analysis. By analyzing the impacts of dextrose, soybean meal as substrate factors, pH, and inoculum level, the medium for maximal production was improved using a "one-variable-at-a-time" strategy. For Serrapeptase production, the coefficient of determination (R2) was determined to be 0.9559, which is statistically significant because R2 ranges from 0 to 1, and 0.9559 is approximately equivalent to 1, implying that the model is correct. With dextrose and soybean meal concentrations of 2.04 (percent w/v) and 2.09 (percent w/v), respectively, maximum Serrapeptase synthesis of 254.65 IU/ml was reported (Vanama J,et.al,2014). To get a maximum production of 85U/gds from Streptomyces hydrogenans, chose 1 percent soybean meal as the best nitrogen source (Nageswara S,et.al,2016). The Gelatin Clearing Zone (GCZ) of Serrapeptase produced from Serratia marcescens demonstrates maximal Serrapeptase production with a clearing zone of 36mm at a gelatin concentration of 0.5 percent w/v, with higher or lower gelatin concentrations resulting in Serrapeptase production decreasing (Mohankumar A, Raj RHK., 2011).The ideal substrate concentration for maximum Serrapeptase yield of 85 U/gds from Streptomyces hydrogenans is 5 g horse gramme (Nageswara S,et.al,2016).

The impact of various carbon sources on STP protein creation by Serratia marcescens. the best carbon hotspot for STP protein creation was glucose. At the point when the Serratia marcescens involved glucose as a carbon source, the STP compound creation came to the most extreme delivering 35mm GCZ. The other carbon sources gave frail or no STP compound creation.

3.5 Effect of UV:

Mutations can be caused in a variety of ways, the most common of which being UV radiation exposure. Serratia marcescens isolates were exposed to UV light for 20, 40, and 60 seconds in a study, and the highest hydrolysis of casein was seen at 20 seconds of UV exposure at 32°C (Manal K M., 2015). Another study found that at 20 seconds of UV exposure, Serrapeptase activity peaked at 1575.3 EU/ml (Ayswarya A,et.al,2013). Streptomyces is also thought to be a good Serrapeptase producer. Streptomyces isolates were given a nitrous acid-treated chemical mutation, which resulted in a 60.1 percent increase in activity above the wild-type strain. When the same strain was UV mutated with a 220 V, 40 W, 50 Hz UV lamp and exposure times of 0, 30, 60, 90, 120, 150, 180, 240, and 360 s, it was discovered that the UV mutant had 33.9 percent more activity than the wild-type strain (Vanama J,et.al,2014). The serratia marcescens produce a 2171EU/ml in wild strain and 2812EU/ml in mutant strain (Shreya Gopinath,et.al, 2020).

3.6 Effect of inhibitor and metal ion:

The movement of S6-protease continuously diminished by expanding a few inhibitors fixation including EDTA, phenanthroline and PMSF, yet with various levels. The best inhibitors were 10mM EDTA, which diminished the protease movement to 11.2 % (49 U/ml) trailed by 5mM EDTA (17.5% (76 U/ml)) and 1mM EDTA (24% (104 U/ml)), when contrasted with the control (refined water). 10% Tween 20, diminished the enzymatic movement to 37.2% (162 U/ml), trailed by 5% and 1% which gave 37.7% (164 U/ml) and 38% (166 U/ml) movement, individually. Then again, the most un-powerful inhibitor was the PMSF, where10mM, diminished the movement to 88.7% (386 U/ml) trailed by 5mM and 1mM which gave 96% (418 U/ml) and close to 100% (431 U/ml) movement, separately. The movement of protease delivered by the chose Serratia strain was affected by the presence of specific particles in the maturation media The protease movement expanded in presence of all tried mono and divalent particles (2.0mM), with the exception of Fe+2, Ca+2, Cu+2, Co+2 and Mg+2 which diminished the protein action when contrasted with the control (refined water). Zn+2 was the most productive particle for expanding the action. It came to 118% (513 U/ml) when contrasted with the control (Ahmed Ammar,et.al, 2019).

4. APPLICATION OF SERRATIOPEPTIDASE ENZYME:

4.1 Serratiopeptidase as a anti biofilm agent:

A community of microorganisms embedded by self-producing matrix of a proteinaceous compound and they are attached to surface. Biofilm is a highly resistant to antibiotic and immune system (P.V. Gupta, M.S. Nagarsenker,2015). One of the trademark properties of biofilms is high protection from the versatile and intrinsic invulnerable frameworks as well as resistance to high centralizations of anti-microbial/antimicrobial specialists. This leads to industrious contamination, making these elements a clinical and monetary aggravation. It is responsible for variety of infection such as UTI, endocarditis, chronic lung infection, osteomyelitis etc. Protease enzyme act as a solubilization of biofilm. Serratiopeptidase enzyme it can alter the virulent phenotype of bacteria and it is very effective against the mature biofilm. Enzyme effective against cell surface protein (R. Mukherji,et.al, 2015).

4.2 Serratiopeptidase as anti-inflammatory agent:

However, serratiopeptidase has been demonstrated to be a viable calming particle in many investigations, endeavor are expected to improve its portion in light of the application. thought about the counter inflammatory impact of serratiopeptidase with anti-inflammatory medicine and other proteolytic compounds trypsin and chymotrypsin in pale skinned person rodents against carrageenan prompted paw edema. Serratiopeptidase showed better mitigating action alone as well as displayed a synergistic impact with anti-inflammatory medicine in both intense and subacute models of irritation in rodent. Serratiopeptidase reduce the in 3 ways. It was hydrolysing the insoluble protein such as fibrin, during injury thinning the fluid that increase the tissue repair system, it degrades pain promoting substance like amine (Sellman S., 2003).

4.3 Fibrinolytic agent:

When tissue is damaged blood vessel release some platelets factor and thromboplastin and it will convert into insoluble fibrin clot is stop the blood transfer, oxygen transfer and cause brain strokes, myocardial infarction and other disease (Guyton A., 1974). Serratiopeptidase enzyme is dissolve a in soluble fibrin clot. Serratiopeptidase is remove any proteinaceous compound that is adhere to arterial wall such as plaques, fatty cholesterol and calcium (Nieper H A., 2010).

4.4 Analgesic:

Serratiopeptidase is hydrolyse or degrade bradykinin, serotonin, histamine that is responsible for oedemic response (Malshe P C, 2000). Bradykinin bind to the Zinc binding site of Serratiopeptidase and enzyme cleave a peptide bond in bradykinin and reduce the pain (Kaviyarasi N S, Suryanarayan V S.,2016). Serratiopeptidase was found to calm agony in patients with root trench treatment and control toothache when emulsified with clove oil.

5. CLINICAL SIGNIFICANCE OF SERRATIOPEPTIDASE

Sr. No.	**Clinical use**	**Symptoms**	**Symptoms treated**	**Reference**
1	Cystic breast disease	Breast engorgement	Reduction in breast pain, swelling and induration	Kee WH,, et. al, 1989
2	Sinusitis/ bronchitis	Hypersecretion of thick mucus	Reduction in the viscosity of the mucus improving the elimination of bronchopulmonary secretions	Shimura S,et.al, 1983
3	Microbial infections	Biofilm-embedded bacteria	Significant improvement in rhinorrhea, nasal stuffiness, coryza and paranasal sinus shadows	Aratani H,et.al, 1980

4	Carpal Tunnel syndrome	Musculoligamento us strain of the hand and wrist	Improvement in pain and inflammation	Panagariya A, Sharma AK., 1999
5	Arteriosclerosis	Partial or complete blockage of the blood flow through an artery	Improvement in blood flow through an artery	Bracale G, Selvetella L., 1996
6	Periodontal disorders	Periodontitis	Serratiopeptidase improves microcirculation and reduces pain	Maheshwari M,, et. al, 2006
7	Osteoarticular infections	Pain in joints, difficult movement	Reduction in pain and swelling	Okumura H,, et. al, 1977
8	Obstetrics	Post-partum Haematomas, breast engorgements and pregnancy related thrombophlebitis	Reduction in pain and swelling	Selan L, , et. al, 1993

6. APPLICATION IN VARIOUS DISEASES

6.1 Cystic Breast Disease:

Additionally, fibrocystic breast disease has been successfully treated with serrapeptase. 70 patients who complained of breast engorgement were randomly assigned to a treatment group and a placebo group in a double-blind research. When it came to reducing breast pain, breast swelling, and breast induration, serrapeptase outperformed the placebo (firmness). Patients who were given serrapeptase reported moderate to significant improvement in 85.7% of cases. Serrapeptase-related side effects weren't reported. Thus, it was determined that using serrapeptase to treat breast engorgement was both secure and efficient (Kee WH, et.al, 1989) .

6.2 Sinusitis/Bronchitis:

Serrapeptase has been demonstrated in clinical research to be beneficial in the treatment of chronic sinusitis, bronchitis, and other airway diseases (Nakamura S,et.al,2003).In patients' nasal cavities, thick mucus is overproduced, which is a sign of sinusitis. Mucus is discharged less frequently as a result of this thickening. Muco-active medications are typically administered in respiratory disorders to reestablish the physicochemical properties of the mucus in order to restore respiratory function. However, some of these medications deplete mucus in a functional way, whereas serrapeptase changes the flexibility of mucus without depleting it (Tomoda K, Miyatam K, 1972). Serratiopeptidase (30 mg/day orally for four weeks) was tested on adult patients with chronic sinusitis to see how it affected the suppleness and viscosity of their nasal mucus. Serrapeptase has been shown in more clinical studies to be effective in treating the symptoms of chronic sinusitis. In one trial, a placebo or the active serrapeptase was used to assess 140 individuals with acute or chronic ear, nose, and throat diseases. After three to four days and at the end of the course of treatment, patients taking serrapeptase noticed a considerable decrease in the intensity of pain, amount of secretion, purulence of secretions, difficulty swallowing, nasal dysphonia, nasal blockage, anosmia, and body temperature.

6.3 Carpal Tunnel Syndrome:

An inflammatory condition (musculoligamentous strain) of the hand and wrist known as carpal tunnel syndrome is marked by severe, protracted pain, inflammation, and impairment. It requires the longest amount of time to recover of any occupational hazard. Surgery and NSAIDs are the usual treatments. Serratiopeptidase reduced the swelling and pain associated with carpal tunnel syndrome in a promising pilot trial. 65 % of the patients displayed clinical improvement. No harmful side effects were noticed (Panagariya A, Sharma AK. , 1999).

6.4 Cardiovascular Implications:

Hans A. Nieper, a Hannover, Germany-based internist, conducted the first study on serrapeptase's impact on plaque buildup in the arteries. Plaque is created when fatty substances, cholesterol, cellular waste materials, calcium, and fibrin (a blood clotting substance) are deposited on the inner lining of arteries. serrapeptase would gradually break down atherosclerotic plaques.

6.5 Dentistry:

Serratiopeptidase aids in improved management of inflammation and tooth infections. Tetracycline administered as periodontal gel has been reported to work well in conjunction with this. (Maheshwari M,et.al, 2006).

6.6 Obstetrics and Gynecology:

Serratiopeptidase's anti-inflammatory properties aid in the healing of pregnancy-related thrombophlebitis, breast engorgements, and post-partum haemorrhages. Male genital infections can also be successfully treated with serratiopeptidase because it improves antibiotic penetration and microcirculation in these organs, which are notoriously difficult to treat with antibiotics (Selan L, et.al, 1993).

7. PHARMACOKINETIC

After the administration of Serratiopeptidase it is spread through the blood stream (Moriya N,et.al, 1994) (Moriya N,et.al,2003). But due to as peptide the enzyme will degrade in gastrointestinal tract and low penetration power due to hydrophilic nature of protein (Woodley JF., 1994) (Swarbrick J, Boylan JC,2002).

So, this the enzyme low use in therapeutically. The enzyme is administered in rate by orally. To check the concentration in plasma at ≥ 30 mg/ kg dose and in lymph at ≥ 1 mg/ kg dose. It was seen that at dose of 100mg/kg concentration in plasma is 0.87±0.41 and in lymph 43±42 ng/ml, and this concentration disappear after 6hours. It was concluded that the Serratiopeptidase absorb from the intestine and riched in inflammatory site via plasma and lymph. With a 1:1 molar binding ratio with the plasma protease inhibitor alpha-1 macroglobulin (a1M), it forms a complex in rat blood that serves to hide its antigenicity while retaining 20% of its initial caseinolytic activity (Kakinuma A,et.al,1982).However, neither the precise dose necessary for its therapeutic activity nor the pharmacokinetic data, such as its oral bioavailability in humans, are reported elsewhere (Shivani Bhagat,et.al, 2013).

8. DOSING

For adult the dosage of Serratiopeptidase enzyme is 10mg 3 times daily (15 to 60mg /day) after meal. As anti-inflammatory agent it takes up to 2 weeks and as mucolytic agent it takes up to 4 weeks. Some oral form of Serratiopeptidase enzyme is enteric coated for protection against the various pH in stomach and small intestine. The dose of 5 to 10 mg of Serratiopeptidase is equal to 10,000- 20,000 unit of enzyme.

15 – 60 mg / day dose use for reduce swelling and pain, 30 – 60 mg/ day dose use for ENT infection as a mucolytic agent.

9. SIDE EFFECTS

Serratiopeptidase can taken in to a short time for clinical trial. If it take long term many serious problem detected like eosinophilic pneumonitis, bullous pemphigoid, Haemorrhage in a patient with Behcet disease, and possibly Stevens-Johnson syndrome by serrapeptase (Longhi C,et.al,2008). There are restricted Unfavourable medication responses detailed such a longways for Serrapeptase. They incorporate skin conditions like dermatosis, dermatitis, erythema, muscle and joint throbs, coagulation anomalies There may likewise be certain gastric related issues like queasiness, anorexia, stomach upset, hack, pneumonitis. Serrapeptase may likewise cause granulomatous hepatitis (just 1 case revealed up until this point), intense eosinophilic pneumonia. Serrapeptase might instigate discharge and henceforth while consuming this medication or any proteolytic medications to forestall apoplexy, draining gamble ought to be taken into thought. It has no inhibitory impacts on prostaglandins and is liberated from genuine impacts like stomach ulceration, joint obliteration, kidney issues, stomach annoyed, mental issues (Sasaki S,et.al, 2000).

10. CONCLUSION

Serratia marcescens produce Serratiopeptidase enzyme by using different medium and optimization of all parameter for highest production. It is very use full in variety of disease treatment due to its anti inflammatory, anti-bacterial, fibrinolytic, analgesic effect. This enzyme used to treat chronic sinusitis, migraine, fibrocystic breast disease, asthma, ovarian cysts etc.

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