Int J Pharm Bio Sci 2015 April; 6(2): (B) 981 - 988

Review Article **Biochemistry**

International Journal of Pharma and Bio Sciences **ISSN 0975-6299**

A REVIEW ON SOMATOSTATIN & THAUMATIN: THE TWO PROTEINS- A GROWTH ATTENUATOR AND A SWEETNER

S. SHAIKH*[1], M. GAMIT[2] AND R. TRIVEDI[3].

[1 2 3] Department of Microbiology, Shree Ramkrishna Institute of Computer Education and Applied Sciences, Athwalines, Surat-395001, INDIA.

ABSTRACT

Somatostatin and its receptors have a critical role in mammalian growth through their control pattern of secretion of growth hormone, but the evolutionary history of somatostatin and somatostatin receptors are ill defined. To date, we have identified a minimum of two genes of somatostatin and five somatostatin receptor genes in mammalian species with variable forms. Its clinical application has been limited by its very short half-life, necessitating continuous intravenous infusion. Octreotide is an 8 amino acid synthetic analogue of somatostatin that possesses similar pharmacological effects. It has a much longer duration of action, however, and can be given subcutaneously. Both the intravenous and subcutaneous routes of injection of octreotide are well tolerated. Octreotide inhibits gastroenteropancreatic secretion, especially of insulin, glucagon, pancreatic polypeptide, gastric inhibitory polypeptide, and gastrin. Thaumatin, a mixture of protein first isolated from the Katemfe fruit. Thaumatin which is about 100,000 times sweeter than sucrose on a molar basis. Thaumatin has potential use a low calorie sweeter for industrial application. Thaumatin is highly digestible protein. Thaumatin has been crystallized in four different forms: orthorhombic (1.75 Å), monoclinic (2.60 Å), tetragonal (1.75 Å) and hexagonal (1.60 Å).

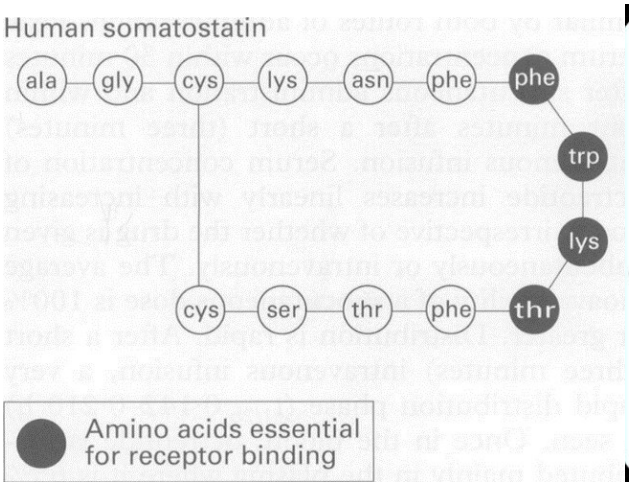
KEYWORDS: Somatostatin, Octreotide, Thaumatin, Thaumatin like protein, Microgravity, crystallization

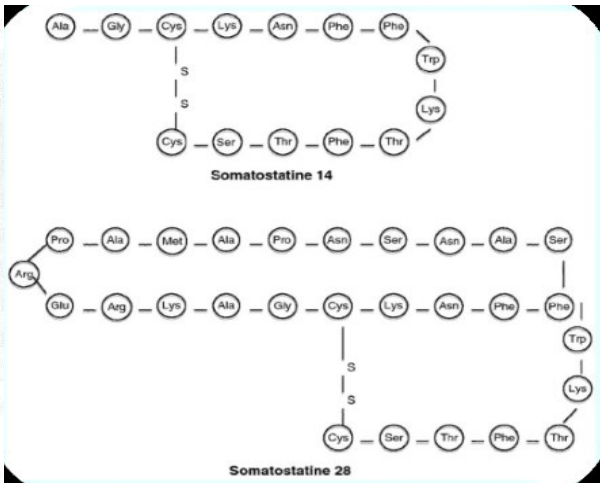
S. SHAIKH
Department of Microbiology, Shree Ramkrishna Institute of Computer Education and Applied Sciences, Athwalines, Surat-395001, INDIA.

***Corresponding author**

INTRODUCTION

Somatostatin (abbreviated as SST) can also be termed as SRIF (somatotropin release inhibiting factor) is a polypeptide secretory hormone first isolated by Brazeau *et al*. in 1973 from the tissue of mammalian hypothalamus. Basically the secretory hormone is somatostatin 14, structurally a tetradecapeptide. It has been found out accidentally while searching for growth hormone releasing factor. The hormone was found to inhibit growth hormone (GH) secretion. In mammals, the growth hormone inhibiting hormone-SRIF was found to be multifunctional polypeptide that is commonly distributed throughout central nervous system and peripheral tissues[1, 2].Originally the molecule is having cyclic arrangement joined by two intramolecular disulphide bonds between the two cysteine residues (Figure). Reduced sequence is linear, however, has got same biological activity as that of cyclic form *in vitro* – that is cyclic form cannot be recognised by specific somatostatin receptors.





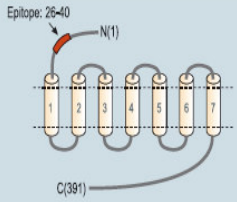
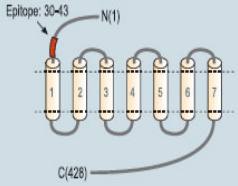
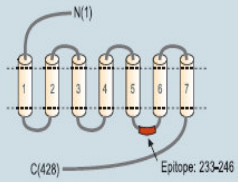
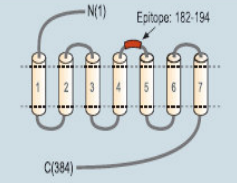
Somatostatin (Somatostatin 1), in mammals is present in two predominant biologically-active forms: SRIF-14 & SRIF-28. The later one, is having NH_2- terminal extension of 14 amino acids as compared to somatostatin 14. Both forms are encodesd by a common gene and obtained from a single precursor[3]. Second native form has been found in 1980[4]. SRIF-28 either may act as a precursor or works as the hormone in its own right, with a bit different mode of action in other tissues. Somatostatin 28 supresses the GH secretion for longer duration but not in case of gastric acid. Somatostatin 28 virtually does not exist in stomach & duodenum, but shows dominance in lower gut[5, 6]. Somatostatin secretion, in neural and peripheral secreting cells can be activated by depolarization and increasing Ca^{+2} concentration[7, 8, 9].SST secretion can be stimulated by number of hormones, neuropeptides, neurotransmitters, cytokines, growth factors and nutrients. Taken into consideration, growth hormone-releasing hormone (GHRH), neurotensin and corticotrophin-releasing hormone (CRH) are all potent stimulators of SST secretion in several tissues. In contrast to that, neurotransmittersopiates and γ aminobutiric acid (GABA) are inhibitors SST secretion. SST action can be mediated by of G protein-coupled receptors' (GPCR's) with somatostatin receptors (SSTRs) with six subtypes, encoded by separate genes except SSTR2A[7]. On the basis of structural characteristics and pharmacological properties, and keeping in view with their sequence homology, the receptor subtypes can be classified into two subgroups, SRIF1 and SRIF2[9].SRIF 1 is having receptors like SSTR2, SSTR3 and SSTR5 whereas SSTR1 and SSTR4 are included inSRIF2 group.

THE SOMATOSTATIN RECEPTOR FAMILY

SST works on the multiple cell targets by a family of six receptors that originally arises from five genes: SSTR1, SSTR2a, SSTR2b, SSTR3, SSTR4, and SSTR5. Upon splicing SSTR2 on C-terminus produces SSTR2a & SSTR2b variants having a bit different tissue distribution.Humans are having only one

somatostatin gene, SST. Somatostatin exerts control over insulin and glucagon.

Table 1
Shows somatostatin receptor family & their tissue distribution

Receptor	Ligand	Tissue distribution	Antibodies	Epitopes
SSTR1	SST-14 > SST-28 CST	Brain, Pancreas (β cells) GI tract, Several human tumors.	Anti-SSTR1 (#ASR-001) Extracellular	
SSTR2a	SST-14 > SST-28 CST	Brain, Pituitary gland, Pancreas (α cells) GI tract, Adrenal gland, Immune cells, Several human tumors.	Anti-SSTR2 (#ASR-006) Extracellular	
SSTR2b	SST-14 > SST-28 CST			
SSTR3	SST-14 > SST-28 CST	Brain, GI tract, Liver, Spleen, Several human tumors.	Anti-SSTR3 (#ASR-003) Intracellular	
SSTR4	SST-14 > SST-28 CST	Brain (less than the other subtypes), GI tract, Lung, Heart, Placenta, Several human tumors.	Anti-SSTR4 (#ASR-004) Extracellular	
SSTR5	SST-28 > SST-14 CST	Brain, Pituitary gland, Pancreas (β and δ cells), GI tract, Several human tumors.	Planned	

SSTR: Somatostatin Receptor; SST: Somatostatin; GI tract: Gastrointestinal tract.

LOCALISATION OF SOMATOSTATIN

Large amounts of somatostatin are found in the gastrointestinal system, including the pancreas, visceral autonomic nervous system, endocrine cells, and gut lumen. Immuno cytochemical studies show that somatostatin localised to the D cells of the pancreas and gut mucosa, particularly in the gastric fundus, antrum, and duodenum[10, 11]. D cells are situated in the lower third of the crypts, from where they extend cytoplasmic processes along the basal membranes to the basal pole of neighbouring glands[12] SSTR expression can be modulated by several factors. First, as in most GPCRs, ligand binding to the receptor induces either receptor internalization and/or uncoupling of the receptor from the G-proteins resulting in receptor desensitization. Second, several hormones such as estrogen and thyroid hormone can regulate SSTRs expression in several tissues at the transcriptional level. Besides their expression in normal tissues, SSTRs have been identified in tumor cell lines of different etiology including pituitary, pancreatic, breast and hematopoietic. Moreover, the majority of human tumors do express SSTRs, often more than one receptor subtype. In general, SSTR2 is the most common SSTR subtype found in human tumors followed by SSTR1 with SSTR3 and SSTR4 being less common. SSTR5 appears to be more tumor specific with strong expression in some tumors (i.e. breast) and complete absence in others (i.e. pancreatic) [13, 14].

ACTIONS

Somatostatin has long recognised inhibitory effects on pancreatic endocrine and exocrine secretion - that is, on insulin, glucagon, and

pancreatic polypeptide[15, 16]and also on pancreatic enzyme and bicarbonate responses to cholecystokinin and secretin[17, 18, 19].It also inhibits the secretion of a wide variety of stimulatory gastrointestinal hormones[20],and decreases gastrointestinal motility and blood flow[17-24].

STRUCTURE-FUNCTION RELATIONS OF SOMATOSTATIN

The action of native somatostatin is brief and rapid, and is followed by rebound secretion, all of which suggests that it inhibits release rather than synthesis, perhaps by depressing exocytosis[25].Somatostatin receptors have been identified in the exocrine pancreas, on islet cells secreting insulin, glucagon and somatostatin[26], and on gastric cells[27]. Intracellularly, somatostatin achieves its effects by cyclic AMP dependent and independent mechanisms[28, 29] and may act by affecting calcium transport through the cell membrane[30]. Because somatostatin inhibits many aspects of cellular function, including endocrine secretion, muscular contraction, and cellular growth, it must antagonise a variety of intracellular signalling programmes. The dephosphorylation processes crucial for secretory activity intimately participate in inhibition by somatostatin at the molecular level. After binding to its receptor, somatostatin probably acts as a dephosphorylator to inhibit secretory processes, but whether the hormone also interacts with DNA to affect transcription is disputed. Because of its many diverse physiological effects, native somatostatin has been investigated for the treatment of acromegaly and gut endocrine tumours. Despite its many potential uses, however, the clinical applications of somatostatin were limited by a very short half-life of two to three minutes, necessitating continuous intravenous infusion and resulting in rebound hyper secretion of hormones after infusion.

SOMATOSTATIN FUNCTION IN HEALTH AND DISEASE

SST and SSTR function has also been involved in several pathological conditions such as Alzheimer's disease, neuroendocrine dysfunctions and several types of cancer. In fact, the expression of SSTRs in several human tumors was so pervasive that it helped create an entire new field in oncology: peptide therapy. More than fifteen years ago a synthetic radiolabeled SST analogue was used to localize neuroendocrine tumors and its metastasis *in vivo* by scintigraphy, a technique where binding of the radiolabeled peptide to the SSTR could be detected as hot spots by γ camera scan[31]. The technique is still considered the most accurate for the diagnosis of cancers of neuroendocrine origin. SST analogues have also been used in direct tumour reduction with 90Y radiolabeled analogues and in the symptomatic treatment of hormone secreting tumours[14, 32]. Somatostatin inhibits many aspects of cellular function, including endocrine secretion, muscular contraction, and cellular growth, it must antagonise a variety of intracellular signalling programmes. The dephosphorylation processes crucial for secretory activity intimately participate in inhibition by somatostatin at the molecular level. After binding to its receptor, somatostatin probably acts as a dephosphorylator to inhibit secretory processes, but whether the hormone also interacts with DNA to affect transcription is disputed.

THAUMATIN

Thaumatin is intensely sweet tasting protein produced in the arils of the fruit of the Africa shrub. In the rainforests of West Africa the herbaceous plant of *Thaumatococcus daniellii* grows. In West Africa the fruit of *Thaumatococcus daniellii* has been traditionally used as a sweetener of palm, wine, corn, bread, and sour fruit. Thaumatin which is, about 100,000 times sweeter than sucrose on a molar basis. Thaumatin has powerful efficacious use as a low-calorie sweetener for industrial applications and could be useful in clarifying the mechanisms of the perception of sweet taste[33]. Plant Thaumatin consists of five extremely sweet forms, with two major group components of Thaumatin I and Thaumatin II and other three are minor group of components like Thaumatin a, b and c.

BIOCHEMICAL AND PHYSICAL PROPERTIES OF THAUMATIN

Thaumatin I and Thaumatin II, both contain a single polypeptide with 207 amino acid

residues and have a basic character as manifested by isoelectric points above 11.5. The amino acid sequence for Thaumatin II has been deduced from its nucleotide sequence[34] and a gene for Thaumatin II has been cloned from messenger RNA derived cDNA. The five amino acids in the Thaumatin II sequence which differ from the Thaumatin I sequence (N46K, S63R, K67R, R76Q, and N113D). The presence of eight disulfide bridges which is stabilized, for tertiary structure of Thaumatin also which makes it unusually stable with respect to heat and pH[35]. Molecular weight of Thaumatin is approximately 22 kilo Daltons. Thaumatin is very much soluble in water (up to 20%) and is also fairly soluble in ethanol/water mixture. It is however insoluble in most common organic solvent such as acetone.

CRYSTALLIZATION OF SWEET PROTEIN THAUMATIN

The Thaumatin has been crystallized in four different forms like (1) orthorhombic (1.75 Å), (2) monoclinic (2.60 Å), (3) tetragonal (1.75 Å) and (4) hexagonal (1.60 Å) [36-39]. By using hanging drop vapour diffusion method from polyethylene glycol as a precipitating agent which form a crystal forms of Orthorhombic and monoclinic[36, 38]. By vapor diffusion method in the presence of 1 M sodium, potassium tartrate containing 0.1 MADA (sodium-N-2-acetamido-iminodiacetic acid) at pH 6.5 forms a tetragonal crystal. *(McPherson 1999)*. These crystals were similar to one grown from ammonium sulphate solution[37]. Thaumatin has also been crystallized in hexagonal crystal form from a tartrate and glycerol containing solution after shifting temperature from 293 K to 277 K [39].

Expression of recombinant Thaumatin

The limited availability of Thaumatin from natural plant sources, due to regional cultivation restrictions, has encouraged alternative production method of Thaumatin. So far, recombinant Thaumatin I and II have been expressed see below in table 2.

Table 2
Show host range, producing recombinant Thaumatin

Host	Promoter[a]	Secretion	Yield	Sweet phenotype	Reference
E.coli	Trp/Lac	No	Very low	No	34
S.cerevisiae	Pgk	No	Low	No	38
B.subtilis	α-amy	Yes	1mg L^{-1}	Yes	40
S.lividans	β-gal	Yes	0.2 mg L^{-1}	?	41
A.awamori	Gla	Yes	5-7 mg L^{-1}	Yes	42

[[a] Trp/Lac: E.coli tryptophan and lactose promoters, Pgk:S.cerevisiae 3-phosphoglycerate promoter, α-amy:B.subtilis α-amylase promoter, β-gal: S.lividansβ-galactosidase promoter, Gla: A.awamoriA.niger glucoamulase promoter.]

The Thaumatin II gene[34] has been transferred to apple in an endeavour to improve their taste quality and phytopathogen resistance [43]. Also the expression of a Thaumatin II gene under control of the CaMV 35S promoter has been shown to improve plant resistance against pathogen. Produced transgenic cucumber plant expressing Thaumatin II protein that showed an enhance resistance against the pathogenic fungus like *Pseudoperonospora cubensis*. Thaumatin II gene introduce into strawberry produced transgenic line which has significantly higher level of resistance to gray mold like *Botrytis cinerea*. Thaumatin II was also expressed in transgenic potato, tomato, pear, barley and tobacco plants[44].

FUNCTIONAL PROPERTIES

Thaumatin can be used as a sweetener or a taste-modifying protein; Flavour Enhancer and Mouth feel Improvement, Masking Bitterness and off-Flavours.

THAUMATIN LIKE PROTEIN

Originally, based on amino acid sequence characteristics PR (pathogenesis related)protein were divided into five families. Now, this group of proteins has been

extended into 17 families based on amino acid sequence characteristics[45]. Multiple isoforms of Thaumatin like Protein, which belong to the PR-5 family, have been found in the crop species barley (*Hordenum vulgare* L.) [46], rice (Oryza *sativa*) and wheat (*Avena sative*) [47]. They are named after their amino acid sequence and structural similarities to the sweet tasting protein Thaumatin. TLP's (Thaumatin like protein) known as osmotins and permatins. The TLP's plays a variety of roles in the development of seed, fruit and flowers of tissues, and specific TLP's have been shown to protect plants against osmotic stress, pathogen attack and the deleterious effects of freezing[48]. The expression of some TLP's is induced by biotic and abiotic factors, such as microbial infection, osmotic stress, abscisic acid (ABA), ethylene, SA, MJ and elicitore (Kitajima and Sato 1999).

CONCLUSION

Since its discovery more than thirty years ago, much progress has been made in understanding the pathological and physiological function of SST and its receptors. The variety of target tissues and cell pathways involved in the biological functions of SST, promise to keep scientists engaged in this field for many years to come. A better elucidation of the different signalling pathways engaged by the different SSTR subtypes should be attempted, as well as a better understanding of the SSTR subtype tissue distribution in normal and diseased states. For this endeavour highly specific antibodies to both intra- and extracellular epitopes of the different SSTR subtypes will be indispensable. The new insights gained from these studies are eagerly awaited. Thaumatin is sweet testing protein found in herbaceous plant of Thaumatococcus daniellii. Thaumatin consist of five extremely sweet protein like Thaumatin I and II , a, b and c, out this two major group Thaumatin I and II both differ from their amino acid sequences. Also the Thaumatin has been formed four different crystal by hanging drop vapour diffusion method. Now a day's limited availability of Thaumatin can be increased by using recombinant technology and expression of Thaumatin. Today's TLP's used for plays a variety of roles in the development of seed, fruit and flower of tissues, protect plants against osmotic stress, pathogen, deleterious effects of freezing.

REFERENCES

1. Reisine T. Somatostatin. Cell. Mol. Neurobiol. 15, 597–614. (1995)
2. Reisine T. and Bell G. I. Molecular biology of somatostatin receptors. Endocrinol. Rev. 16, 427–442, (1995).
3. Patel Y. C. and Srikant C. B. Somatostatin receptors. Trends Endocrinol. Metab. 8, 398–405, (1998).
4. Praydayrol L, Jomvall H, Mutt V, Ribet A. N-terminally extended somatostatin: the primary structure of somatostatin- 28. FEBS Lett; 109: 55-8, (1980).
5. Descos F, de Parscau L, Olive C, Chayvialle JA. Somatostatin-like immunoreactivity in human gastrointestinal mucosa [Abstract]. 2nd International Symposium on Somatostatin, Athens, 1-3 June (1981).
6. Penman E, Wass JAH, Butler MG, et al. Distribution and characterisation of immunoreactive somatostatin in human gastrointestinal tract. Regul Pept; 7: 53-65, (1983).
7. Patel, Y.C. Front. Neuroendocrinol. 20,157, (1999).
8. Csaba, Z. and Dournaud, P. Neuropeptides 35, 1, (2001).
9. Olias, G. et al. J. Neurochem. 89, 1057, (2004).
10. Polak JM, Pearse AGE, Grimelius L, et al. Growth hormone release inhibiting hormone in gastrointestinal and pancreatic D cells. Lancet; i: 1220-2, (1975).
11. Dubois MP. Immunoreactive somatostatin is present in discrete cells of the endocrine pancreas. Proc NatlAcad Sci USA; 72: 1340-3, (1975).
12. Larsson LI, Goltermann N, De Magistris L, et al. Somatostatin cell processes as pathway for paracrine secretion. Science; 205: 1393-5, (1979).

13. Hofland, L.J. and Lamberts, S.W. Ann. Oncol. 12, S31, (2001).
14. Reubi, J.C. Endocr. Rev. 24, 389, (2003).
15. Adrian TE, Bloom SR, Besterman HS, Bryant MG. PP-physiology and pathology. In: Bloom SR, ed. Gut hormones. New York: Churchill Livingstone, 254-60, (1978).
16. Floyd JC, Fajans SS, Pek S. Physiological regulation of plasma levels of PP in man. In: Bloom SR, ed. Gut hormones. New York: Churchill Livingstone, 247-53, (1978).
17. Boden G, Sivitz MC, Owen OE, et al. Somatostatin suppresses secretin and pancreatic exocrine secretion. Science; 190: 163-4, (1975).
18. Dollinger HC, Raptis S, Pfeiffer EF. Effects of somatostatin on exocrine and endocrine pancreatic function stimulated by intestinal hormones in man. Horm Metab Res; 8: 74-8, (1976).
19. Konturek SJ, Tasler J, Obtulowicz W, et al. Effect of growth hormone release inhibiting tissue on hormones stimulating exocrine pancreatic secretion. Jf Clin Invest; 58: 1-6, (1976).
20. Arnold R, Linkisch BG. Somatostatin and the gastrointestinal tract. Clin Gastroenterol; 9: 733-53, (1980).
21. Layer P, VD Ohe M, Muller MK, Beglinger C. Effects of somatostatin on the exocrine pancreas. Scand Jf Gastroenterol; 26: 129-36, (1991).
22. Bloom SR, Ralphs DN, Besser GM, et al. Effect of somatostatin on motilin levels and gastric emptying [Abstract]. Gut; 16: 834, (1975).
23. Konturek SJ, Krol R, Pawlik W, et al. Pharmacology of somatostatin. In: Bloom SR, ed. Gut hormones. New York: Churchill Livingstone, 457-62, (1978).
24. Wahren J, Felig P. Influence of somatostatin on carbohydrate disposal and absorption in diabetes mellitus. Lancet; ii: 1213-5, (1976).
25. Kraicer J, Spence JW. Release of growth hormone from purified somatotrophs: use of high K+ and the ionophore A23187 to elucidate interrelations among Ca^{++}, adenosine 3', 5'monophosphate and somatostatin. Endocrinology; 108: 651-7, (1981).
26. Mehler PS, Sussman AL, Maman A, et al. Role of insulin secretagogos in the regulations of somatostatin binding by isolated rat islets. Jf Clin Invest; 66: 1334-8, (1980).
27. Reyl F, Silve C, Lewin MJM. Somatostatin receptors on isolated gastric cells. In: Rosselen G, Fromageot P, Bonfils S, eds. Hormone receptors in digestion and nutrition. Amsterdam: Elsevier, 391-400, (1979).
28. Bausher LP, Horio B. Neuropeptide Y and somatostatin inhibit stimulated cyclic AMP production in rabbit ciliary processes. Curr Eye Res; 9: 371-8, (1990).
29. McNellis EL, Bausher LP. Stimulatory and inhibitory cyclic AMP responses in rabbit ciliary processes after cervical ganglionectomy. Curr Eye Res; 10: 399-407, (1991).
30. Luft R, Efendic S, Hokfelt T. Somatostatin: both hormoneand neurotransmitter? Diabetologia; 14: 1-13, (1978).
31. Krenning, E.P. et al. Lancet 1, 242, (1989).
32. Kaltsas, G.A. et al. Endocr. Relat. Cancer 12, 683, (2005).
33. Masuda, T. & Kitabatake N. J. Biosci. Bioeng. 49. 4937-4941, (2006).
34. Edens L, Heslinga L, Klok R et al. Gene; 18 (1): 1-12, (1982).
35. Iyengar, R,B., Smits, P., Van der Ouderaa, F.J.G., Van der Wel.,H, et al., The complete amino acid sequence of the sweet-tasting protein Thaumatin I. Eur. J. Biochem, 96, 193-204, (1979).
36. McPherson A, Weickmann J: X-ray analysis of new crystal forms of the sweet protein thaumatin. J.Biomol. Struc. Dyn. 7, 1053-1060, (1990).
37. McPherson A: Crystallization of biological macromolecules. Cold Spring Harbor Laboratory Press, NewYork, (1999).
38. Lee, JH, Weickmann, JL, Koduri R. K.Ghosh –dastidar, P. et al., Expression of synthetic Thaumatin genes in yeast. Biochemistry, 27, 5101-5107, (1988).
39. Charron C, Giege R and Lorber B: Structure of thaumatin in a hexagonal space group: comparison of packing

contacts in four crystal lattices. Acta Cryst. D60, 83-89, (2004).
40. Illingworth, C., Larson, G., Hellekant, G., Secretion of the sweet-tasting plant proten Thaumatin by Bacillus subtilis. Biotech.Lett. 10,587-592, 1988.
41. Illingworth, C., Larson, G., Hellekant, G., Secretion of the sweet-tasting plant proten Thaumatin by Streptomyces lividans.J.Ind.Microbiol, 4, 37-42, (1989).
42. Faus, I., del Moral, C., Androer, N., del Rio, J.L. et al., Secretion of the sweet tasting protein Thaumatin by recombinant strains of Aspergillus niger var. awamori. Appl. Micribiol. Biotechnol, 49, 393-398, (1998).
43. Dolgov SV, Schestibratow KA, Moniteiro S. Acta Hort; 663 (1): 507-10, (2004).
44. Pushin, A. S., Ovchinnikova, E. V., Shulga, O. A., Firsow, A.P., Dologov, S.V., Accumulation of a super-sweet protein Thaumatin II in apoplast of tobacco transgenic plants Biotechnology, 31-40, (2008).
45. S.Muthukrishnan, H. George Liang, Harold N. Trick & S. Bilkram Gill, Plant cell, Tissue and Orgen Culture. 64-93, (2001).
46. E.Reiss and C, Horstman, Physol.Mol Plant., 58-183, (2001).
47. J Hejgaard, S Jacobsen, I Svendsen. FEBS Ketters, 291, 1, 127, (1991).
48. An Lovar, S and M. Dermastia. The comparative analysis of osmotins and osmotic like PR-5 proteins. Plant Biol. 5: 116-124, (2003).
49. Kitajima, S and F, Sato. Plant pathogenesis related proteins molecular mechanisms of gene expression and protein function J.Biochem. 125: 1-8, (1999).