

## Beneficial and toxicological response of Oxytocin with stability, detection, marketing and authorization: *a receptor mediate Approach*

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### ABSTRACT

Peptide hormone Oxytocin has the distinction of being the first among the peptide hormones to be sequenced and biochemically produced. Oxytocin is involved in a wide spectrum of activities from milk letdown, parturition, ejaculation and erection to social, sexual and maternal performance. Since of the spectrum of its meanings it has been used therapeutically for conditions by performing the Oxytocin receptors (OR) mediate activity, oxytocin are connected by means of Gq proteins which enrolled to GTP revive the action of Phospholipase-C enzyme. Due to gives rise and activation one by one biochemical consequences occur that activate the Phospholipase-C enzyme at the end. The Phospholipase-C enzyme responsible by means of produce 1, 2-diacyl glycerol along with Inositol triphosphate, Inositol triphosphate grounds release intracellular basis Ca<sup>2+</sup> ions, which in turn origins a direction of cellular process. Oxytocin being credible agent to excited the plant growth in variable aspects. The redeployment of macrobiotic and micro biotic nutrients among tissues and seeds of plants proved beneficial results in terms of plants anatomy and physiology with certain toxicological and beneficial response by means of stability, detection, marketing and authorization in diverse way.

**Keywords** : Oxytocin, stability, detection, marketing and authorization, toxicology

## I. INTRODUCTION

Oxytocin is a neurosecretory peptide hormone which is also known as  $\alpha$ -Hypophamineis a posterior pituitary or neurohypophysial hormone exuded by M-cells it means (meganocellular, neurosecretory) cells in supraoptic and paraventricular nuclei of the hypothalamus. It is stored in posterior pituitary in anticipation of its discharge into blood flow. As, it is a

peptide hormone, it is constituted of several amino acids. Oxytocin is constituted of nine amino acids that's why it is often called as nanopeptide, amino acids are bonded with disulfide link in between cystine residues 1 and 6. At 8<sup>th</sup> position a neutral amino acid leucine is present while basic amino acid arginine is present at equivalent position in case of vasopressin which is also known as antidiuretic hormone. At 3<sup>rd</sup> position isoleucine is necessary to

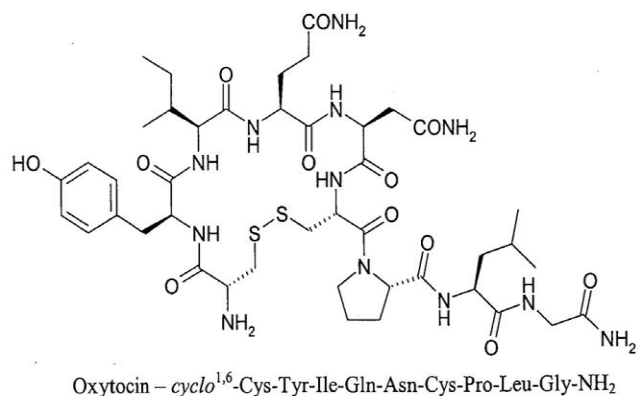
stimulate the oxytocin receptors [1]. In the year 1835, the great Italian scientist Nicholas Farraze discovered oxytocin. It has a chemical formula of  $C_{43}H_{66}O_{12}N_{12}S_2$ . Commercially oxytocin is available as intravenous and intramuscular injections along with as nasal sprays for a variety of principle [2].

To be sequenced and manufactured biochemically, oxytocin hormone have a peculiarity of being earliest in the midst of polypeptide hormones [1]. Electrical activity of the oxytocin cells in the hypothalamus regulates discharge of oxytocin from neurosecretory nerve ends. Oxytocin scheming vesicles release the hormone through exocytosis by getting basic nerve action or potential which is transmitted toward the nerve endings behind the axons. Earlier than the discharge of oxytocin, it needs to be cleavage of *Neurophysin-I* molecule. Such crucial step is completed by a series of enzymatic actions. At last the most important mechanism means hydrolysis, is catalyzed by the enzyme *peptidylglycine  $\alpha$ -amidatingmonooxygenase*, which discharge the biologically dynamic oxytocin [3]. For regulatory effect, oxytocin by binds to specific cell exterior receptors through a phosphoinositide signaling pathway (PISP). It is in list of schedule H drug, it is low-priced and offered gamely [4]. For instigation of milk in females and maintenance of labour as well as for induction, oxytocin is secreted endogenously within all mammals. Given that oxytocin be a nanopeptide hormone, so that it vanish swiftly from the blood stream within the timing of 2-6 minutes due to action of a variety of biocatalyst. For that particular reason the chemically synthesized oxytocin is generally employed in human and veterinarian medicine [5]. Oxytocin may play a role in autism and may be an effective ailment relining in favor of autism's repetitive and affinitive functions [6]. More currently, intranasal entry of oxytocin was recorded to up reach emotion recognition in youngsters diagnosed with autism [7]. As per autistic subjects

after recovery by means of inhaled oxytocin, display extra suitable behavior related to socialism. But research suggests some task, for next clinical researches of oxytocin are needed to represented beneficial and toxicological effects in the treatment of excess oxytocin results [8].

## II. Oxytocin : Biochemistry

In India the schedule drug oxytocin, is a inexpensive as well as fluently available, here it is forenamed as Schedule H-drug [9]. The sequence of oxytocin is basically represented by chain of nine amino acids as cysteine-trysteine-isoleucine-glutamine-asparagine-cysteine-proline-leucine. So, in term of molecular weight oxytocin is a relative short polypeptide, as constituted of nine amino acids [10]. Unambiguous set of proteins is present on the membrane of the responding cells; therefore action by oxytocin is performed using these specific proteins group. They are known as the oxytocin receptors (OR). The oxytocin receptors (OR) is a seven trans membrane domain polypeptide. It belongs to the Rhodopsin-type, class-I, G-Protein Coupled Receptor Family [11]. Oxytocin receptors (OR) are connected by means of Gq proteins. Gq is a subtype of G-proteins. It get connected to GTP which rouse the activity of Phospholipase-C enzyme. With attachment of oxytocin to OR, it gives rise to a series of biochemical episodes that activate Phospholipase-C enzyme at the end. Phospholipase-C enzyme activities, involved for generating inositol triphosphate and 1, 2-diacyl glycerol. Inositol triphosphate causes liberation of intracellular  $Ca^{2+}$  ions, which in turn causes an array of cellular events [12].



**Figure 1.** Structural representation of Oxytocin

### III. Oxytocin: stability and estimation

A technique signifying stability is an authorized quantitative and systematic method which distinguishes the variation with time interval in the chemical, physical, or biochemical properties of the chemical substance and drug product that are specific with the intention that the contents of dynamic ingredients, deprivation products, and overall components can be perfectly measured with negligible obstruction.

According to International Council for Harmonization (ICH) stability involves accomplishment of strained decomposition under various conditions such as pH value, presence of light, oxidative agent, heat and separation of drug from deprivation products. Requirement and validation of analysis of deprivation products and overall by products, apart from the dynamic ingredient is basic headline of stability signifying technique [13]. The stability signifying technique is probable that consent to analysis of deprivation products.

In the same consequences of stability studies of oxytocin another study reported oxytocin explicit stability demonstrating isocratic HPLC technique in the presence of deprivation products and chlorobutanol [14]. In a further study, an optimized pitch reverse phase HPLC technique was developed

and authorized to identify and separate a mixture of deprivation products of biochemical oxytocin [15].

### IV. Lab stability

As per instruction of International Council for Harmonization Q1A (R2) for stability clearly requires accomplishment of required forces for decomposition under a diverse medium and condition for instance pH value, presence of light, oxidative agent, heat and separation of drug from deprivation products. The oxytocin with concentration 200 IU/mL with pH value 3.5, kept at different temperatures for about 3-4 years were analyzed repeatedly for biochemical changes. Concentrates kept under low temperature give you an idea about no loss of oxytocin. Samples under 21°C expressed quite small loss of activity concerning (1.5 percent/year). Samples under 30°C expressed a striking loss (about 10 percent/year). With dilute injections of oxytocin similar outcome were obtained. Thus it concluded that oxytocin should not be exposed to higher temperatures and oxytocin in solution has a shelf life of about 3 years under temperature 21°C. [16]. Further study carried out by World Health Organization in alliance of IDA Foundation, two different batches of three different trademarks of oxytocin ampoules were hoard at different temperatures and samples were examined for oxytocin content more than a period of 2 years [17].

### V. Oxytocin for plant growth

Various literatures support that oxytocin being persuasive agent to excite plant growth. Redeployment of macrobiotic and micro biotic nutrients among tissues and seeds prove to be the basic supremacy of oxytocin that possibly improves the plant growth and development. For breaking dormant stage, stimulation of germinating stage and further growth of the germ cells oxytocin is used. The major role of oxytocin is to regulate cell cycle and cell

division; it means it to some extent control plants cell life and thus control plant growth and its development [18]. Perhaps due to existence of meristematic tissue in explants as a consequence, it signify its role as a morpho-dogmatic biochemical in plants thus by regulation of cell cycle oxytocin invigorate upshot on hypocotyl dimensions [18].

Now-a-days oxytocin is being utilized by the farmers for the superfluous growth of various fruits and vegetables like brinjal, gourd, pumpkin, watermelon, and cucumber to attain maximum market rate [19]. Amongst fruits and vegetables oxytocin is principally exercised in cucurbits in order to enlarge its dimension with mass of the fruits, suddenly by fast biochemical action. If oxytocin is regularly included in diet through fruits and vegetables the biochemical hormones oxytocin may prove foundation for severe injurious disease to mankind. Some of major defects include sterility, malfunction of nervous system, heart disorders, and defects in memory power [20].

By the action of biochemical, mostly it is enviable to stimulate plant growth rather than stimulation of weed growth. As a result, there is an urgent requirement for finding an inexpensive resource which efficiently stimulates plant development and growth rather than to stimulate weed growth. Active plant hormones are the fundamental key for stimulation of plant growth. For instance, active plant hormones such as abscisic acid, auxins, gibberellins and cytokinins are some basic hormones to stimulate the plant. Being expensive and presence of toxicants are major quandary among these agents in order that they are relatively harmful with their higher concentration. On the other hand, for inhibiting weed growth various kinds of weedicides and herbicides like phenoxy acids can be used [21]. Derived plant component and its production of are influenced by oxytocin under invitro investigation in the pharmacological sectors on behalf of biomass

accretion the influence of oxytocin as concentration ( $100 \text{ mgL}^{-1}$ ) over and above on the making of glycyrrhizin, are documented, mean related phytoconstituent of liquorices being utilized.

High concentration of toxicants is the major crisis due to chemical contents of weedicides and herbicides. Consequently, for such reason a large number of these chemicals have been banned in order to avert from its harmful side defects. By using oxytocin as an invigorating mediator for plant growth we can come over from all such problems. On the other hand oxytocin is an inexpensive agent. It is produced in the human body. In comparative to plant hormones it is highly persuasive and invigorating agents that affect plant growth [21].

Improvement of the nutrient circulation, transport and discharge through roots apex with enhanced photosynthesis rate is the basic mechanism of biochemical response of oxytocin synthetic peptide. This means redistribution of macrobiotic and micro biotic compounds involving tissues and various plants storage cell is the key mechanism of synthetic oxytocin's action. Oxytocin stimulates germination in seeds, nevertheless most expected yield and translocation of macrobiotic material to root apex and embryo shoot from the nucleus. Oxytocin functionally utilized for breaking of dormant stage, stimulation of germination stage and the growth of the germ cells. Under short time and stimulated condition the plant will complete better cycle with weed. Further, it can manipulate flower primodium and seeds by insertion of macrobiotic substances with an augmented substitution of nutrients and organic compounds to the seeds. Certainly it may escort to more harvests with expected quality. With effect of quick germination, oxytocin may bring new result within next generations causing extra and improved growth due to stimulation in seed composition [21].

## VI. Oxytocin: Detection in fruits and vegetable

For detection of presence of oxytocin and harmful biochemical adulterants in fruits and vegetables, wireless sensors proved as best source of technology. Liquid chromatography mass spectrometry is the method which is extensively used to scrutinize the presence of oxytocin in solution, mammalian plasma, raw materials, and milk. The wireless sensors are not used for the exposure of oxytocin in fruits and vegetables. The principle of refractometer and glucometer was introduced which intended to detect oxytocin in fruits and vegetables [10]. Very simple appliances which facilitate measurement of nutritional content of fruits and vegetables is known as refractometer while glucometer is another appliance which is utilized for determination of the glucose concentration level, whether it is high, low, or accurate [10].

Radio immune examine (RIE) with enzyme immune examine (EIE) method are about thousand times more sensitive as compared to the HPTLC method and their employed protocols. To compute physiological stages in blood, tissues of animals and humans following method is used. Being expensive and the inaccessibility of radioactive technique are certain restrictions in this method. That's why it is suggested that HPTLC method should be used for detection of active hormones such as oxytocin in case of fruits and vegetables. The concentration of the oxytocin content in samples after that, has been

endeavor to target oxytocin content in the exposure limit of HPTLC method. The literature reviews on various vegetables, fruits and milk, highest amount of adulteration was found in vegetables while in fruits maximum concentration of oxytocin was present in watermelon ( $75.25\mu\text{gkg}^{-1}$ ) while in milk sample least amount ( $39.10\mu\text{gkg}^{-1}$ ) oxytocin concentration was present. But, adulteration was not founded in the samples of brinjal and papaya. Oxytocin is being used by vegetable growers to increase their yield, as it is believed that this hormone increases the size of their produce. The use of this hormone in water melon is widely reported. However, whether consumption of such vegetables and fruits causes any deleterious effects on the consumers remains to be seen. Current investigation illustrates that the HPTLC method has simple process, rapid identification, economic sustainability, and specificity that can be functional for usual examination of oxytocin content [19].

## VII. Oxytocin: Presence and sample analysis

For sample testing standard solution of oxytocin is prepared by suspending 1 mg of oxytocin and 100 ml methyl hydroxide. Further the stock solution 5 ml is diluted to 50 ml for preparing testing solution that is used for sample testing. Various samples were collected from different of Agra, India. After analysis result as each observation there is somewhat positive or negative accuracy factor (table 1).

**Table 1.** Analysis of commodity samples to examine oxytocin content ( $\mu\text{g}/\text{kg}$ ) [19].

S. No.	Commodity Sample	Oxytocin in HPTLC plate	Oxytocin Content	Average Oxytocin Content
1.	Watermelon	S <sub>1</sub> = 18.31 S <sub>2</sub> = 19.35 S <sub>3</sub> = not detected S <sub>4</sub> = 19.03	S <sub>1</sub> = 73.25 S <sub>2</sub> = 77.43 S <sub>3</sub> = not detected S <sub>4</sub> = 76.12	75.25+2.27( $\mu\text{g}/\text{kg}$ ) 75.25 -2.27 ( $\mu\text{g}/\text{kg}$ )
2.	Bottol gourd	S <sub>1</sub> = 12.60 S <sub>2</sub> = 13.07 S <sub>3</sub> = 12.00 S <sub>4</sub> = 11.65 S <sub>5</sub> = 11.22	S <sub>1</sub> = 50.40 S <sub>2</sub> = 52.30 S <sub>3</sub> = 48.00 S <sub>4</sub> = 46.60 S <sub>5</sub> = 44.90	48.4 + 2.45( $\mu\text{g}/\text{kg}$ ) 48.4 + 2.45( $\mu\text{g}/\text{kg}$ )
3.	Milk	S <sub>1</sub> = 10.22 S <sub>2</sub> = 9.55 S <sub>3</sub> = 9.77 S <sub>4</sub> = not detected S <sub>5</sub> = 10.23	S <sub>1</sub> = 40.89 S <sub>2</sub> = 38.20 S <sub>3</sub> = 39.09 S <sub>4</sub> = not detected S <sub>5</sub> = 40.92	39.10+2.20( $\mu\text{g}/\text{kg}$ ) 39.10 - 2.20( $\mu\text{g}/\text{kg}$ )

### VIII. Biochemical adulterants: A rhyme for human disease

The basic food products for the human use are fruits and vegetables that are vastly nutritious. As they have low shelf existence and are highly fragile. Various organic and inorganic chemicals as calcium carbide, synthetic hormones and oxytocin being used in fruit and vegetable for unnatural ripening of fruits as well as increasing the size of fruits and vegetables by using biochemical adulterants or toxic biochemical these food products are informed of being unhygienic and lethal. Under PFA rules, 1955 calcium carbide is a carcinogenic agent and got banned. Being a pesticides ethephon is suggested as artificial ripener. Oxytocin is used in unmarked fruits and vegetables for increasing its size and volume. But excessive use of such chemical may cause severe health issues.

According to ministry of agriculture ethylene gas only is used in low concentration with 10-100 ppm exogenously to activate ripening. Depending upon the crop species and its maturity condition it may be safe if concentration vary from 0.001-0.01%. The increasing concentrations of oxytocin in human body can cause nausea or vomiting, it affects mental balance, and can cause cough severe headache, hallucination, hypertension and anxiety. These symptoms can create a disorder that finally led to a disease. Excess concentration of pictocin (oxytocin derivate) and pesticides in fruits and vegetables so prove harmful for mankind [2].

### IX. Impact of oxytocin in human as variable toxicological response

#### (1). Oxytocin in vision and retinal toxicity

Being vital for launching vision contact and involve in trust for individuals oxytocin always interact with retinal membranes. For that reason oxytocin hormone

is always control to children who have an effect of autism through intranasal squirts. Also, some autism influenced children were conferred a placebo of saline intranasal squirt. Administering oxytocin based drugs to boost their trust. The children were found to set up improved vision and they commence to convict people better than children who were governed with a placebo [20].

### **(2). Oxytocin and sexual activity as spontaneous erectile responses**

Impulsive erectile responses were noted as biochemical oxytocin was over seeded to male rats. Oxytocin enrolls to have sexual excitement in both male and female sexes. Oxytocin also boosts the erectile response in male ejaculation of male spermatid cells. In females it also increases sexual intercourse duration and so that female observes a feeling of trust, satisfaction and sexual desire. However females who are not excited to have sexual activity with their corresponding person oxytocin create a sense of irritation [1, 9].

### **(3). Uterus and Uterine inner movements**

Uterine contraction and its inner movement are an uncommon role of oxytocin. During the delivery and event of labour pain then progesterone level falls and the normal oxytocin level (NOL) causes cervical dilation, thus causing pain. The release of oxytocin, increasing cervical dilation show the way to parturition [2]. Liquid chromatography mass spectrometry (LC-MS/MS) is widely used for monitoring the presence of oxytocin in an aqueous solution, mammalian plasma, raw materials, and milk.

### **(4). Mammalian lactation and reproduction**

With stimulation of sucking, impulses are transferred to hypothalamus to release oxytocin as the nipples of mammary gland of female get sensitized. High amount of the hormone are released by the contractile apparatus of the alveoli which cause the milk

ejaculation by “let down reflex” action. Frequent use of oxytocin resulted in various reproductive disorders in both cattle and buffalo, including follicular ovarian cysts (18.33%), luteal cysts (28.33%), retention of placenta (11.66%), repeated estrus (25%) in buffalo and follicular cysts (26.66%), luteal cysts (23.33%), retention of placenta (8.33%), repeated estrus (23.33%) [21].

### **(5). Oxytocin in maternal circulation**

At the time of delivery and cervical dilation the affection take place between the child and mother, due to high level of oxytocin secretion in the maternal circulation. Thus oxytocin is often known for induction of maternal characters [22]. It generates affection among people and stronger the bond of child and mother. The research conducted by administering of oxytocin in female rats shown evidence of increased maternal circulation and when virgin rats were injected with the same hormone also they exhibit same results. At the same time if mother rats were injected with oxytocin inhibitors, they did not express any maternal behavior with their own off springs. Same studies were founded in human also [23, 24]. Harmful effects of milk obtained after oxytocin injection studies under the multiple researches and obtain their findings and conclusion. The reports on the harmful effects of milk produced by oxytocin treated dairy cattle are misleading, whether secreted endogenously response of oxytocin to natural stimuli or administered exogenously, oxytocin produces the desired impacts within under monitoring timing and it was found that it gets metabolized fastly, lead to inactive the products [25].

### **(6). Oxytocin in behavior and physiological response**

Various studies shows that oxytocin is secreted during gratifying condition for example hugging with our close relative and during the exciting contact of a male and female who are interacted for each other. As oxytocin is secreted by hypothalamus and is

accumulated in posterior pituitary gland therefore some extents of secretion depends on the limbic system also. The discharge of oxytocin causes initiation of contentment that's why it shown to perform same biochemical action. It has a propensity to adjust our brain signals which is responsible for expressions, which is incredibly imperative for processing of physiological responses [25]. As per above justification oxytocin perform and initiate basic trust, bond between mother and her child, love making, parturition, milk discharge, erection of reproductive organs of males and spermatid discharge, also balances the stress and relieve from anxiety [26, 27].

#### Oxytocin: Marketing and authorization

As per data provided by manual for Procurement and Supply of Quality Assured MNCH Commodities' some of the oxytocin and its injection marketing company and authorized holder along with their registration number are mentioned in table 2.

**Table 2.** Oxytocin products manufacturer and authorized holders with registration number.

S. NO.	Products	Authorized holder	Registration number
1.	Pitocin (oxytocin injection, 10 IU/mL)	Par Sterile Products LLC, USA	NDA #018261
2.	Syntocinon 10 IU/mL injection ampoule	Novartis Pharmaceuticals Australia Ltd, Australia	AUST R 13383
3.	Oxytocin Aspen 10 IU/mL injection	Sandoz Ltd, Australia	AUST R 162499
4.	Oxytocin injection	Fresenius Kabi, USA	NDA #018248
5.	Oxytocin 10 IU/mL solution for infusion	Peckforton pharmaceuticals Ltd, UK	PL 15760/0036

Oxytocin may have merit as an agent to remove the residual milk and udder debris, during the treatment of mastitis, as prior removal of these substances from the udder should enhance the local impacts of antibiotics used during the treatment. Profitable impacts of oxytocin on autism, improving trust in relationships, dampening social anxieties, attractions between opposite sexes, but it remains to be seen and recorded their claims pass the test of laboratory [28-30]. Effects of oxytocin on plant growth parameters such as percent seed germination, root length and hypocotyl length on economically important spice and source of edible oil, *Brassica campestris* was studied in current research. In a report of survey conducted by the Uttar Pradesh state of India, about the variable misuse of oxytocin.

#### X. Conclusion

Although oxytocin be a potential peptide natural and artificially synthesized hormone, to perform receptor mediate approaches and mechanisms, which appeared as biochemical changes in organism anatomically as well as physiological aspects, peptide nature of oxytocin can induce growth of fruits and vegetables along with beneficial and certain harmful impact on human also. However its excessive use can cause severe health problems in human in certain ways. The beneficial and toxicological response of oxytocin along with stability, their proper detection, marketing formulation and legal authorization all the reactivity shown and expressed by the basis of a receptor mediate approach.

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