

## Category: Pro-Sexual Nutrient for Male-Sexual-Dysfunction [FSSAI Category]

### Introduction

Deranged libido, erection and orgasm are only a part of the male sexual dysfunction. However, many individuals in the present day scenario are unsuspecting victims of a disorder which destroys the life of males who are afflicted by this disorder. Premature ejaculation occurs when a man ejaculates sooner during sexual intercourse than he or his partner would like. Premature ejaculation is a common sexual complaint. Estimates vary, but as many as 1 out of 3 men say they experience this problem at some time. As long as it happens infrequently, it's not cause for concern. Both psychological and biological factors can play a role in premature ejaculation.

### Simplified diagnostic criteria for premature ejaculation

- i. Ejaculation that always or nearly always occurs prior to or within about 1 min of vaginal penetration
- ii. Inability to delay ejaculation on all, or nearly all, vaginal penetrations and
- iii. Negative personal consequences, such as distress, bother, frustration and/or the avoidance of sexual intimacy

### Symptoms of Premature Ejaculation [PE]

The primary symptom of premature ejaculation is the inability to delay ejaculation for more than one minute after penetration. However, the problem may occur in all sexual situations, even during masturbation in males. Premature ejaculation can be classified as lifelong (primary) or acquired (secondary). Lifelong premature ejaculation occurs all or nearly all of the time beginning with the first sexual encounter. Acquired premature ejaculation has the same symptoms but develops after having previous sexual experiences without ejaculatory problems.

### Possible Causes

The exact cause of premature ejaculation isn't known. While it was once thought to be only psychological, doctors now know premature ejaculation is more complicated and involves a complex interaction of psychological and biological factors.

### Psychological Causes

Some doctors believe that early sexual experiences may establish a pattern that can be difficult to change later in life, such as:

- i. Situations in which the individual hurries to reach climax in order to avoid being discovered
- ii. Guilty feelings that increase the individuals tendency to rush through sexual encounters

Other factors that can play a role in causing premature ejaculation include:

- i. **Erectile Dysfunction** - Men who are anxious about obtaining or maintaining an erection during sexual intercourse may form a pattern of rushing to ejaculate, which can be difficult to change.
- ii. **Anxiety** - Many men with premature ejaculation also have problems with anxiety either specifically about sexual performance or related to other issues.
- iii. **Relationship Problems** - If the individual has had satisfying sexual relationships with other partners in which premature ejaculation happened infrequently or not at all, it is possible that interpersonal issues between the individual and his current partner are contributing to the problem of premature ejaculation.

## Biological Causes

A number of biological factors may contribute to premature ejaculation, including:

- i. Abnormal hormone levels
- ii. Abnormal levels of chemicals called neurotransmitters in the human brain
- iii. Abnormal reflex activity of the ejaculatory system
- iv. Certain thyroid problems
- v. Inflammation and infection of the prostate or urethra
- vi. Inherited traits

## Risk Factors

1. **Erectile Dysfunction** - At increased risk of premature ejaculation if you occasionally or consistently have trouble getting or maintaining an erection. Fear of losing your erection may cause you to consciously or unconsciously hurry through sexual encounters.
2. **Health Problems** - If you have a serious or chronic medical condition, such as heart disease, you may feel anxious during sex and may unknowingly rush to ejaculate.
3. **Stress** - Emotional or mental strain in any area of your life can play a role in premature ejaculation, often limiting your ability to relax and focus during sexual encounters.

## Premature Ejaculation Treatment

A range of drugs are currently used by clinicians for the management of PE including antidepressants, local anesthetic agents and phosphodiesterase type 5 inhibitors. Whether the medication is used regularly or on demand is an important consideration for patients when choosing the most appropriate drug for the treatment of their PE. An on-demand drug offers the flexibility of using the medication just prior to sexual intercourse, thereby reducing the risks of side effects associated with the drug for the rest of the time.

Data so far suggest that generally speaking the benefit of on-demand dosing is inferior to the benefits seen with regular dosing. On the other hand, daily dosage allows for a more spontaneous sexual experience. Set against this, regular dosing results in greater exposure to the drug and may be associated with more pronounced side effects. Research has shown a majority of men preferred a daily regimen as opposed to an on-demand regimen. Moreover, the stigma associated with the daily use of an antidepressant (i.e. selective serotonin reuptake inhibitors [SSRI]) may be a complicating factor in the compliance of patients to the treatment.

A recent introduction into the Indian market is a short acting on-demand SSRI Dapoxetine. The major problem with this medication is that it has to be taken at least 1-2 hours prior to the sexual act. In a country like India, planned sex is virtually impossible, as the culture and custom are different unlike the western world. Although many Physicians consider this drug relatively safe and with few side effects, the major side effects that have been observed are nausea, diarrhea, headache, dizziness, decreased libido, erectile dysfunction [ED] and severe delays in ejaculation on long term use.

A common feature amongst all the medications is the side effect profile that include fatigue, nausea,

dizziness, dry mouth and hypotension, erectile dysfunction [ED] and decreased libido. The desensitizing creams that are applied to the penis are usually messy, cause skin irritation, numbing of the vagina, and erectile dysfunction [ED]. Although PDE5 inhibitors do not have a direct effect on PE, they have been used with little success for erection and have exhibited side effects that include headache, flushing, nausea, change in color visualization or perception.

Physicians have been battling and trying hard to find a solution to PE of either Primary or Secondary origin. As for Primary PE, the treatment regimen is for a lifetime, but for Secondary PE a combination of drugs needs to be administered with multiple side effects. Psychotherapy and counseling as secondary measures have met with little success.

The successful use of a nutraceutical, Hypericum containing Hypericin and Hyperforin [St. John's Wort] in Psychiatry paved way for the use of this active ingredient in a recipe along with other ingredients such as Butea superba, Piper longum, Turnera diffusa and Crocus sativus for treating premature ejaculation. The safety profile of these ingredients has been documented and has produced good clinical results in individuals with PE. This combination of nutraceutical ingredients has been aptly titled **Lvate**. The combination, of these ingredients has improved patient compliance and also the need for multiple drug therapy, thereby eliminating the unwanted, adverse drug reactions.

Lvate is available in a vegetable capsule, facilitating the release of the active components at the site of dissolution, without being exposed to the gastric contents.

**Each Vegetarian Capsule of Lvate Contains -**

Herbal Extracts Standardized to:	Quantity in mg
333 micrograms of Hypericin and 14 mg Hyperforin [Hypericum perforatum]	300
20% Piperine [Piper longum]	100
Extract of Leaf Turnera diffusa	100
Extract of Root Butea superba	50
Extract of Stigma of Crocus sativus	10

**Clinical Pharmacology [Summary of the Ingredients & MOA]**

The summary of the MOA of the active ingredients is as follows:

Ingredients	Action Exerted
Hypericum perforatum [St. John's Wort]	Inhibits the re-uptake of several synaptosomal [nerve junctions]neurotransmitters such as Serotonin, Noradrenaline and Dopamine. The active constituents, Hypericin and Hyperforin exert an action similar to that of SSRIs [Selective Serotonin Re-uptake Inhibitor]. Hyperforin extract produced rapid onset of action and increased ejaculatory latency time in men with baseline ejaculatory latency of less than or greater than two minutes. There is an overall improvement in the sexual satisfaction score in both the male and female partners. A nutraceutical , which shares therapeutic efficacy similar to synthetic SSRI.
Piper longum	Piperine, the active component, exhibits adaptogenic property [reduces stress] and exerts mild antidepressant activity due to regulation of neurotransmitters in the central nervous system that include Nor-epinephrine, Dopamine, and Serotonin.
Turnera diffusa	The active constituent/s improve libido and erection and also exert mild anti-anxiety.
Butea superba	Contains Flavanoids that improve libido, erectile function, sexual vigor and prolongs the duration of penile erection.
Crocus sativus	The extracts of the stigma contain Crocin & Saffronal the active constituents that improves sexual desire, increases the number of erectile events, while exerting a mild anxiolytic activity.

**Absorption**

Despite the mechanism of action being elucidated for all the active ingredients, the absorption patterns of the individual and the ingredients combined in Lvate have not been studied and documented.

**Distribution**

The distribution pattern of the individual and combined ingredients of Lvate have not been studied.

**Metabolism**

The metabolism and metabolite excretion patterns of the individual and combined ingredients of Lvate have not been studied.

## Elimination

The elimination pattern of the individual and combined ingredients of Lvate have not been studied.

## Carcinogenesis, Mutagenesis

The nutraceutical supplement Lvate has not been administered to pregnant or lactating women as the supplement is currently recommended only for males.

## Indications

Premature or Early Ejaculation of varied aetiology

## Contraindications

No known contraindications; however, in severe cases of renal failure, hepatic failure of any aetiology or males with pituitary or testicular tumors may not be suitable candidates for the use of Lvate capsules.

## Warnings & Precautions

The ingredients of Lvate have been used for centuries, and their active principles for over 2-3 decades. It is advisable to inquire with the patients if they have taken similar nutraceutical preparations or one or more ingredients of the preparation, to prevent any adverse events.

Concurrent administration of synthetic drugs has resulted in drug interactions with no fatalities. The physician needs to be updated on the drug interactions mentioned in drug interactions.

Although one or more of the individual ingredients contained in Lvate is being used in female sexual dysfunction, the drug should not be administered to pregnant or lactating mothers, as the effects of the nutraceutical supplement have not been studied in this population.

Individuals who are consuming Lvate should inform their treating Physician of the other medications they are taking.

## Adverse Drug Reactions

No serious adverse drug reactions have been reported with use of Lvate; however, in susceptible individuals, mild to moderate GI upset has been noted that usually resolves during the course of the treatment. Headache and anorgasmia have been reported in very high doses of 900 – 1500 mg of Hypericum per day.

## Drug Interactions

Drug interactions of mild to moderate severity have been noted with Carbamazepine, Cyclosporine, Nifedepine, Theophylline, Midazolam, SSRIs, and consumption of alcohol.

## Usage in Special Population

1. **Pregnancy & Lactation** – The use and effects of Lvate have not been studied in pregnancy and lactating mothers.
2. **Pediatric Use** – The use/ safety of Lvate has not been studied in pediatric population.

- 3. Renal and Hepatic Insufficiency** – During animal and human clinical studies, no changes were observed in either renal or hepatic parameters. However, it is advisable to avoid the use of Lvate in cases of hepatic or renal failure, as the absorption, metabolism, distribution and excretion patterns of the active ingredients have not been studied in these classes of patients.

### **Dosage And Administration**

The recommended dosage of Lvate is 1-2 Capsules at bedtime with warm milk for a minimum duration of 90 days and thereafter can be extended at the discretion of the treating physician.

The vegetable capsule of Lvate should be swallowed whole and should not be opened or chewed as the active ingredients are in a pellet form in the capsule. A gap of 2-3 hours must be maintained between the consumption of other medications and Lvate capsules to avoid drug interactions.

### **How Supplied**

Each strip contains 10 Vegetable Capsules and each box contains 10 Strips of 10 Vegetable Capsules.

### **Storage**

The carton must be stored at the ambient temperature mentioned on the carton, preferably at temperatures below 25°C, away from direct sunlight. Do not use the drug if the capsules are leaking or damaged.