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# *Mucuna* and Parkinson's Disease: Treatment with Natural Levodopa

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## Abstract

*Mucuna pruriens* is a tropical bean containing large amounts of levodopa and is the most important natural remedy for Parkinson's disease. Famous neurologists have patented methods of extraction for its advantages over the synthetic forms, Sinemet and Madopar. This natural levodopa is less toxic and has a faster and more lasting effect and can delay the need for pharmaceuticals and combination therapies. Currently, there are many patients with Parkinson's disease who take *Mucuna* and spontaneously reduce the dose of conventional drugs and do so behind their doctors' backs. *Mucuna* should always be taken under medical supervision.

**Keywords:** *Mucuna pruriens*, Parkinson's disease, levodopa, natural, treatment, benefit, dyskinesia, conventional

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## 1. Introduction

*Mucuna pruriens* is a species of bean that grows in the tropics. It is very rich in natural levodopa, which is better tolerated and more potent than the synthetic levodopa in Sinemet, Madopar, or Stalevo. *Mucuna* seed extract has been an effective treatment of Parkinson's disease (PD) in many patients. Scientific studies attest to it, and renowned neurologists have patented the specific techniques for extracting levodopa from this plant. They relate to the use of *Mucuna pruriens* seeds for the preparation of a pharmaceutical composition for the treatment of Parkinson's disease to obtain a broader therapeutic window in L-Dopa therapy, to delay a need for combination therapy, to obtain an earlier onset and longer duration of L-Dopa efficacy, and to prevent or alleviate acute and chronic L-Dopa toxicity [3, 44]."

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Meanwhile, patients have recorded their positive experiences with *Mucuna*; they buy it online (no prescription needed) and use it in secrecy without consulting their neurologist. It is used without control, and if there are not more accidents, it is because it is relatively safe (although there are risks if misused), and most of the capsules sold contain very low doses, almost like a diet supplement. The formula at high concentrations is dangerous, especially when mixed with antiparkinsonian drugs. Neither the patients nor the doctors (most of them) have clear ideas about this plant, its ingredients (not only levodopa), the proportions in which it is absorbed, or how to manage it.

## 2. *Mucuna pruriens*: the plant

*Mucuna pruriens* is a kind of “hairy” or furry bean, native to Southeast Asia, especially the plains of India, but also widely distributed in tropical regions of Africa and the Americas (particularly in the Caribbean). The wide dissemination of the plant explains its variety of names, depending on the location: velvet beans, cowhage, itch bean, picapica, Fogareté, Kapikachu, sea bean, deer eyes, yerepe, Atmagupta, nescafe, and chiporazo. *Mucuna* is a legume (such as common beans, peas, lentils, peanuts) and the largest natural source of levodopa.

This annual plant grows as a climbing shrub with long tendrils that enable it to reach more than 15 feet in height. Young plants are almost completely covered by a diffuse orange hair that disappears as they age. It grows or is cultivated as fodder to enrich the soil (adding a lot of nitrogen) or for its medicinal qualities.

*Mucuna* is called “pruriens” because of the intense itching produced by their contact. The orange “hairs” of flowers and pods of *Mucuna pruriens* contain chemicals (including serotonin) that, when they come in contact with the skin, cause intense irritation and itching and sometimes very troublesome injury including allergies and severe swelling.

In India, *Mucuna* has been the main healing herb for three thousand years. All parts of the plant are used in more than 200 indigenous medicinal preparations. The seeds contain up to 7% levodopa, which is used in the treatment of Parkinson’s disease. In the Ayurvedic medicine, velvet bean is recommended as an aphrodisiac, and studies have shown that its use causes a rise in testosterone levels, increased muscle mass and strength, and also improves coordination and attention.

Extract of *Mucuna* seed powder contains large amounts of levodopa and a little serotonin and nicotine along with other ingredients that are only partially known. In the treatment of Parkinson’s disease, such extracts seem to be more effective and less toxic than the synthetic preparations [1].

## 3. *Mucuna*: therapeutic possibilities

The interest in *Mucuna* increased after 1937 when it was discovered that the variant contained large amounts of levodopa. However, this amino acid alone does not justify the many medical applications of this interesting plant.

In the treatment of Parkinson's disease, some results in groups of patients and in experimental animals show that, apart from natural levodopa, *Mucuna pruriens* has other ingredients that show outstanding features. It must contain other substances that improve the absorption of levodopa and metabolic efficiency, as explained below.

To date, 50 substances have been identified in the powder of its seeds [2]. Other still unidentified components must exist in *Mucuna*, such as portions or mixtures of alkaloids, proteins, peptides, polysaccharides, glycosides, glycoproteins, and several phytochemicals including tryptamine, alanine, arginine, glutathione, isoquinolone, mucunine, nicotine, prurienine, serotonin, tyrosine, etc., [3].

These substances, identified or not, confer special powers on *Mucuna*, perhaps boosting the levodopa or adding some kind of dopamine agonism and even extended its effects. We need to continue investigating them.

### 3.1. Strategies to enhance levodopa

Trials have been conducted in which *Mucuna* seeds are germinated in darkness or in different conditions of light and providing varied nutrients (oregano, proteins from fish, etc.). Results showed that by adding oregano to seeds germinated in darkness, *Mucuna* sprouts containing 33% more levodopa have been obtained [4]. Other researchers selected some cells from the ground and then grew them grow in a medium that allows nutrients to be supplied; in this way they have managed successfully to increase the concentration of levodopa [5, 6].

### 3.2. Beneficial effects of *Mucuna*

*Mucuna* is recommended in Ayurveda to treat more than 200 diseases—as a vital tonic, an aphrodisiac, a remedy to reduce stress, a good diuretic, etc.—and is also used against parasites, to control diabetes and lower cholesterol. And, of course, it is a treatment for *kampavata* (the equivalent of Parkinson's disease). Western science seems to confirm many of these effects. *Mucuna* improves libido, semen quality, etc., and even works against snake bites.

*Mucuna* increases the adaptation and regeneration of tissues in general and has been shown to increase growth hormone [7]. It has an anabolic effect and increases muscle mass; it also has antioxidant properties and favors the protective functions of the liver [8].

Diabetics and people with high cholesterol may benefit from *Mucuna* [9]. In rats it has been shown to lower cholesterol by 61%, and glucose was reduced by 39% [10]. *Mucuna* enhances the recovery of diabetic neuropathy induced in animals [11]. In humans it delays the onset of diabetic nephropathy.

*Mucuna* also protects the stomach to relieve gastric mucosal lesions induced experimentally in rats [12]. *Mucuna* contains prurienine which increases intestinal peristalsis and is a good remedy for constipation, so prevalent in Parkinson's disease patients. It usually enhances motility and gastric emptying, although some patients assert otherwise.

### 3.3. Aphrodisiac and antiepileptic

*Mucuna* increases libido, or sexual drive, in men and women due to its dopamine-inducing properties; dopamine is the substance of desire and profoundly influences all appetites. In

male animals *Mucuna* raises testosterone levels and increases sexual activity [13]. In men with fertility problems, *Mucuna* clearly enhances sexual drive and power while improving the quality of the sperm: it increases the number of cells and also gives them greater mobility [14]. It is assumed that it acts on the hypothalamus-pituitary-gonadal axis.

Researchers can cause status epilepticus or catalepsy in experimental animals by various techniques: electroshock, pilocarpine, or Haloperidol. These improve if treated with velvet beans [15].

### 3.4. Snake poison antidote

This is not an exaggeration or a myth. *Mucuna* is a good antidote for snake bites, possibly by a direct effect on the venom, attributed to its glycoprotein antitrypsin content [16] but also because it is procoagulant and prevents cardiorespiratory depression induced by poison.

Specifically, *Mucuna* reduces mortality due to bites from the following snakes: Gariba viper (*Echis carinatus*), Viper Malaya, and spitting cobra (*Naja sputatrix*) [17].

### 3.5. Kampavata is Parkinson's disease

In India there were Parkinson's disease patients three thousand years before the birth of James Parkinson. These were diagnosed as *Kampavata*, a disease characterized by trembling (*Kampa* in Sanskrit). In Ayurveda this process was classified within the group of neurological disorders (*Vata Rogas*) [18, 19].

They obviously lacked Sinemet and Madopar but were treated naturally with levodopa, obtained by crushing *Mucuna* seeds, which they later diluted and administered as a beverage [20]. For thousands of years; this therapy has worked, these patients have improved and, above all, according to that we know, showed fewer side effects than people taking synthetic drugs.

### 3.6. The seeds are cooked in cow's milk

In an interesting clinical trial, 18 Parkinson's disease patients were treated according to the criteria of Ayurvedic medicine. They received a concoction of powder of *Mucuna pruriens* cooked in cow's milk along with other traditional plants (*Hyoscyamus reticulatus*, *Withania somnifera*, *Sida cordifolia*) [21].

The results found that this treatment improved rigidity and bradykinesia; tremor was diminished and cramps subsided; however, sialorrhea (drooling or excessive salivation) worsened. Later, the powder of plants which had been added to the milk was analyzed, and it was found that each dose used contains 200 mg of levodopa [21].

The Hindu *Mucuna* extract contains a small amount of levodopa that fails to justify the significant clinical improvement of parkinsonian symptoms. This suggests that in the *Mucuna*, there are other substances that enhance the role of levodopa (such as carbidopa, entacapone, or tolcapone) or other active ingredients with antiparkinsonian effects [20, 22, 23].

One important thing is guaranteed by Ayurveda: after thousands of years of using these plant extracts, thousands or millions of patients have continued to improve their symptoms without significant adverse effects.

## 4. *Mucuna* works better than Sinemet

In 1978, a publication by R.A. Vaidya in India stated that Parkinson's disease could be treated with extracts of a plant, *Mucuna pruriens*, which contains natural levodopa and is tolerated better than the synthetic version [24]. In the West the scientific writings that described improvement in parkinsonian symptoms after eating *Mucuna* or other beans appear between 1990 and 1994 [18, 25, 26]. These legumes could replace some of the conventional medications. There are some recipes from "Parkinsonian cuisine" that are based on beans [22, 27].

### 4.1. *Mucuna* seed powder

Scientific journals have begun publishing cases of improvement in patients after eating *Mucuna*. The Parkinson's Disease Study Group undertook a multicenter clinical study (in collaboration with several hospitals) with 60 patients, of which 26 took Sinemet before the test and the other 34 were "pharmacologically virgins" (they had never taken levodopa). All were treated for 12 weeks with powder from *Mucuna* seeds: an average of six bags, each containing 7.5 grams, equivalent to 250 mg of levodopa. In other words, each sachet contained the same amount of levodopa as a Sinemet 25/250 but without the carbidopa. Neurologists of four centers screened patients using the appropriate scales (UPDRS) and found considerable improvement that was statistically confirmed [28]. Thus, Ayurveda medicinal recipes have demonstrated their clinical effectiveness.

### 4.2. Zandopa: a medicine with *Mucuna*

This legume seems to work. Investigations gave evidence of this, and *Mucuna* seed powder (called HP-200) was marketed as a drug, under the brand name Zandopa [2]. It was first distributed in India and has been available in the United Kingdom since 2008. Now customers can buy it freely online without a prescription. It is important to be careful, however, because the levodopa dose is relatively high (250 mg per sachet) when combined with carbidopa or other antiparkinsonian drugs.

### 4.3. Improvement in mice doubles or triples

We can experimentally induce parkinsonism (unilateral or bilateral) in rodents via certain toxic substances. Used in these trials, levodopa from *Mucuna* has no side effects and produces an improvement that is double or triple that of the synthetic version [29].

In another experiment, animals ate extract of *Mucuna* for a year. They were then put down, and their neurotransmitters were measured in different areas of their brains. Interestingly, no changes were seen in the nigrostriatal pathway, but dopamine was significantly increased in the cerebral cortex [2]. This has two possible explanations: that natural levodopa is more potent or that *Mucuna* contains other beneficial chemicals.

### 4.4. Improvement in humans

This clinical study [1] complies with the strict requirements laid down by the most rigorous scientific methodology established by the Quality Committee of the American Academy of



Neurology [30]. This was a randomized, double-blind, crossover study which adhered to precise objectives and clearly defined protocols and was carried out by several independent observers.

They studied eight Parkinson's disease patients at (on average) 62 years of age, 12 years after diagnosis with a stage of progression of 3.5 on the Hoehn and Yahr scale. Prior to this test, they were treated with levodopa (572 mg mean value). In addition, patients were taking other previous associated drugs (amantadine, pergolide, ropinirole, pramipexole, or cabergoline) that remain unchanged. All had a rapid response to levodopa (1.5 to 4 hours) along with very disabling motor fluctuations during the morning.

Each subject was hospitalized three times (1 week apart) and went without any medication the night before the test. The next morning, at the same time, each received at random one of three combinations: one dose of 200 mg of levodopa with 50 mg of carbidopa (two tablets of Sinemet Plus) or two or four sachets of *Mucuna* (15 or 30 grams) equivalent to 500 or 1000 mg of natural levodopa (100 or 200 according to the conversion factors).

The results were clearly better in those who take two sachets of *Mucuna* extract: improvement in their symptoms occurred faster, their plasma levodopa levels were higher, and clinical efficacy was more durable. In addition, their dyskinesia was not worsened. The details follow.

#### 4.5. "Citius, altius, fortius et durabilius"

The Olympic motto *faster, higher, stronger* can be applied to *Mucuna*, because, in comparison to Sinemet, it acts more rapidly (34 minutes instead of 68), produces a greater elevation of the plasma level of levodopa (110% higher), and appears to be stronger (the effectiveness of natural levodopa is double or triple that of the synthetic version). In addition, the improvement achieved is more durable (with *Mucuna* the "on" phase is prolonged 37 minutes longer than with Sinemet). Therefore, it can be described as *citius, altius, fortius... durabilius*.

#### 4.6. Twice as effective

We have seen that the *Mucuna* seed extract naturally contains levodopa. If we quantify and compare it to the same dose of synthetic levodopa contained in tablets of Sinemet (or Madopar), we find that levodopa from *Mucuna* is approximately twice as powerful in controlling parkinsonian symptoms [31].

The efficacy of synthetic levodopa (without carbidopa) has been compared to that of natural levodopa (*Mucuna*) using rats with experimentally induced parkinsonism. The natural levodopa proved to be two times as effective at improving symptoms [32]. This test maintained the following proportions: 125 and 250 milligrams of synthetic levodopa were compared with the equivalent dose of natural levodopa (respectively, 2.5 and 5 grams of *Mucuna* powder 5%). Then the test was repeated, this time adding 50 mg of carbidopa to the two types of levodopa. Again, *Mucuna* proved to be more efficient.

#### 4.7. The problem of volume

*Mucuna* is more effective, more rapid, and durable; however, to achieve a dose that will offer the same relief as Sinemet or Madopar, it would be necessary to prescribe large amounts of

seed powder dissolved in liquid [24, 33]. The need to consume seed powder several times a day would soon overwhelm the patient, and the treatment would be abandoned as too cumbersome.

The solution to the problem can be found in concentrated extracts. This allows for the presentation of *Mucuna* in tablets or capsules, facilitating the application of different doses of the product and making it easy to manage daily consumption of *Mucuna* in the amounts deemed necessary. There is another choice that requires the cooperation of the neurologist: *Mucuna* could be used in association with carbidopa to achieve greater efficiency with less seed powder.

#### **4.8. *Mucuna* with carbidopa**

The first trials that compared the effects of Sinemet with *Mucuna* required six or seven daily sachets of powdered seeds. This can be maintained for a few days but becomes quite cumbersome with time. Actually those studies were done to compare natural levodopa (*Mucuna*) to a synthetic combination of levodopa and carbidopa (i.e., the contents of Sinemet).

The solution seems simple: add carbidopa to *Mucuna*. This increases the efficiency of the natural levodopa contained therein and therefore eliminates the need to take large amounts of seed powder. We must be careful when capsules of concentrated extracts are used because the dose can be excessive when you consider that *Mucuna* is more effective than synthetic levodopa.

There are published trials in which *Mucuna* is administered in combination with carbidopa and is compared to Sinemet. Rats with experimentally induced hemi-parkinsonism were treated with powdered *Mucuna* seeds (2.5 and 5 g) associated with carbidopa (50 mg) and in contrast to other groups wherein the equivalent synthetic levodopa dose (125 and 250 mg) was also associated with carbidopa. *Mucuna*-carbidopa proved to be more than twice as effective as Sinemet, and this was found by measuring the rotation contralateral (on the injured side) of the animals in each group [32].

Very recently, a new trial was performed to investigate whether *Mucuna pruriens* (MP) may be used as alternative source of levodopa for indigent individuals with Parkinson's disease (PD) who cannot afford long-term therapy with marketed levodopa preparations. Eighteen patients were included in a double-blind, randomized, controlled, crossover study [34]. It shows that single-dose *Mucuna pruriens* intake met all noninferiority efficacy and safety outcome measures in comparison to dispersible levodopa/benserazide. Clinical effects of high-dose MP were similar to levodopa alone at the same dose, with a more favorable tolerability profile [34].

We know that the carbidopa in Sinemet prevents the peripheral side effects of levodopa (nausea, rapid heart rate) and enhances mobility. It appears that the carbidopa in *Mucuna* is even more effective: it decreases mild side effects and doubles or triples patients' strength [1].

#### **4.9. Other advantages of *Mucuna***

*Mucuna does not produce dyskinesia.* A different study, this time in monkeys (with unilateral parkinsonism induced experimentally), produced very interesting results on the possibility of dyskinesias. One group was treated with Sinemet (levodopa and carbidopa), another with *Mucuna* plus carbidopa, and the third only with *Mucuna*. All the animals experienced an improvement in their symptoms. Dyskinesia was then assessed by the study of spontaneous activity in the substantia nigra. Larger dyskinesia appeared in the Sinemet group. In those



treated with the combination of *Mucuna* and carbidopa, dyskinesia seemed more moderate. Interestingly, in those who had only taken *Mucuna*, no dyskinesia was found [35].

*Long-term Mucuna without dyskinesia.* A similar experiment was performed, but this time *Mucuna* treatment was continuous, extending for a year. It was done in rodents and compared *Mucuna* with Madopar. One group was treated with Madopar (levodopa and benserazide), another with *Mucuna* plus benserazide, and the third only with *Mucuna*. All were controlled for a year. The symptoms were alleviated in all groups, but the improvement was significantly higher in those who were treated with *Mucuna* plus benserazide.

To highlight the results of long-term use: after 1 year, major dyskinesia appeared in rats that had taken Madopar. Rodents treated with *Mucuna* plus benserazide had some minor dyskinesia while for animals that took only *Mucuna*, none at all [36]. Even more, in an experiment with different dyskinesias (those produced by neuroleptics like haloperidol), these repetitive movements improved when *Mucuna* was administered [37].

*Mucuna is neuroprotective.* It seems that natural levodopa from *Mucuna* (or the whole of the components in this legume) is nontoxic and even neuroprotective [38]. This has been demonstrated in mice (with experimentally induced parkinsonism) which were given synthetic levodopa or *Mucuna*. Those treated with *Mucuna* experienced an improvement in most of the symptoms. Also, when they were slaughtered 1 year later for brain analysis, it was found that the endogenous contents of levodopa, dopamine, norepinephrine, and serotonin in the *substantia nigra* were significantly restored [2].

In other studies with rodents, researchers agree that the extract of *Mucuna* clearly is neuroprotective compared to synthetic levodopa [39] or estrogen [40]. They believe that this is due to its antioxidant and chelating activity (processing of iron) and because it avoids mutagenic effects in DNA [41, 42].

Antioxidant and neuroprotective properties of *Mucuna* have also been shown in rodents that were previously damaged experimentally by nerve toxins such as paraquat. The results also highlighted the improvement in habits and cognitive functions of these animals [43].

*Dosage does not increase over time!* It sounds too good to be true: treatment with *Mucuna* does not produce dyskinesia; and it also improves secondary abnormal movements which occur with chronic synthetic levodopa therapy. One more thing, with *Mucuna* it would be not necessary to gradually increase the dose as time goes on, as is the case with those taking synthetic drugs.

Below, I transcribe literally the benefits of *Mucuna* extracts as reflected in the scientific foundations of the patent carried out by Van der Giessen, Olanow, Lees, and Wagner [3]: “Conventional L-Dopa therapy requires a gradual increase of the effective dose over time resulting of progression of disease and/or the neurotoxic effects of L-Dopa or dopamine with an increase of toxic reactions and, over time, the appearance of dyskinesia, increasing in severity with dose. In clinical experiences with *Mucuna pruriens* seed preparations, these negative phenomena have not been observed in that for the effective treatment of Parkinson’s, the dose of *Mucuna pruriens* derived L-Dopa remained relatively stable over longer periods of time, and in that dyskinesia, even in patients with pre-existing dyskinesia following long term therapy with conventional L-Dopa preparations, appeared to be less in occurrence and severity...” [3].

After reading this, it seems strange that *Mucuna* is not yet dispensed in all pharmacies as a revolutionary drug.

#### **4.10. patents of extracts of *Mucuna***

The proprietaries over certain techniques of *Mucuna* extracts—WO 2004039385-A2 [44] and US 7470441-B2 [3]—are very prestigious researchers. They have developed specific techniques to extract various substances from *Mucuna*, not only levodopa. As they have detailed, many of the ingredients are indicated “...for preventing, alleviating or treating neurological diseases,” for general use as “a pharmaceutical combination for neuroprotection or neurostimulation,” and, more specifically, “for the treatment of Parkinson's disease.” They have left little to no chance.

#### **4.11. Zandopa and a cocktail with *Mucuna***

The previously mentioned Zandopa brand from Zandu Laboratories, which owns the patent for *Mucuna* powder product known as HP-200, was used in important clinical trials [28, 45] and has been marketed for several years. Som C. Pruthi has patented [46] a combination from the Ayurveda tradition that mainly contains *Mucuna* (between 55 and 99%), together with *Piper longum* and *Zingiber officinale*. He described a woman diagnosed with Parkinson's disease at age 51 that did not tolerate conventional medicines. She took Pruthi's combination of *Mucuna* for 12 years. In this long period, it was found that progression of the disease was very slow and side effects were not detected.

#### **4.12. An extra-concentrated extract**

The drawback of *Mucuna* powder and primitive extracts is the large volume of legume one needs to consume in order to achieve sufficient blood levels of levodopa. This produces over-eating and gastrointestinal upset and causes many to abandon this therapy. To avoid this trouble, Manyam has patented a method [47] involving the removal of grease from the cotyledons of the seeds. Using ethanol as a solvent, the concentrated extract is isolated and finally freeze-dried.

With this technique, it is possible to process 2.5 kilograms (over 5 pounds) of *Mucuna* powder, which is then reduced to just 46 grams (1.6 ounces). In this conversion the relative proportions of levodopa are maintained (or even increased). So the amount of vegetable to be ingested is reduced to less than 2%. In this way, it can be supplied as tablets, capsules, or syrup and even diluted for injection [47]. On the other hand, its efficacy has been demonstrated in vitro and in animals: when this concentrated extract is supplied to rats with “induced parkinsonism,” their symptoms improve twice as much as the treatment with synthetic levodopa [32].

#### **4.13. More benefits than conventional levodopa**

The foundations of the patent, based on the references provided, reveal that, in relation to standard levodopa-carbidopa medications (Sinemet) or levodopa-benserazide (Madopar), the extracts of *Mucuna* have important advantages that confirm those listed in the previous chapter.

*Mucuna* has a wider therapeutic window: the range of dosage in which a drug can be used without causing toxic effects. That means that there is a large margin between the minimally effective dose of *Mucuna* and one that could cause damage in the body.

Patients get better sooner with it. Researchers gave patients a tablet of Sinemet, and they noticed the “on” effect after 54 minutes. But when they took *Mucuna*, they were already active after only 23–27 minutes [1]. In addition to being quick-acting, *Mucuna* (at a dose of 30 grams) has been found to be effective for longer durations: patients were still “on” for 204 minutes after taking the seed extract, beating Sinemet tablet by half an hour [1].

Neither acute nor chronic toxic effects have been described. Even with high doses of *Mucuna*, there were less adverse effects (nausea, abdominal discomfort) than in patients who received the equivalent of the conventional drugs [3]. Other long-term studies of *Mucuna* (in monkeys and rats) have shown that the dreaded dyskinesia and other symptoms associated with continuous treatment with levodopa are lower and in some cases even tend to improve [35, 36].

#### 4.14. Other benefits of *Mucuna*

According to the application for the patent, *Mucuna* alone may suffice to relieve patients' symptoms for a period of time, and therefore combination therapy (levodopa plus agonists) can be delayed. Even more, these renowned specialists believe that *Mucuna* extracts may be useful in the treatment of multiple neurodegenerative processes: chorea, Parkinson's and Alzheimer's diseases, and vascular dementia [3]; further applications include many other metabolic disnutritional disorders and, systemic, endocrine and autoimmune disturbances (vitamin deficiency, lupus, demyelinating, etc.), as well as neurotoxic, ischemic, or traumatic injuries [44].

Anecdotally, a woman with white hair has been described that after 3 months of treatment with *Mucuna*, it turned back to black [50], “like when I was young,” she said. This is food for thought: the threads connecting youth, dopamine, suffering, old age, stress, and gray hair [48, 49].

#### 4.15. *Mucuna* is more than levodopa

The available data has shown that *Mucuna pruriens* has special properties that distinguish it from synthetic levodopa. These data provide a basis for the patent registered by Olanow and Lees (quoted *verbatim*): “the *Mucuna pruriens* formulation seems to possess potential advantages over existing commercially available synthetic L-Dopa formulations in that it combines a rapid onset of action with a comparable or longer duration of therapeutic response without increasing dyskinesias or acute LD toxicity in spite of much higher LD plasma levels...” [3].

Natural ingredients (known or unknown) combined with levodopa may contribute to improvement of parkinsonian symptoms and reduction of dyskinesia [44]. This opens up the anticipation of important therapeutic progress and the hope of further studies to confirm that extracts of *Mucuna* seeds are a safe and effective alternative [35]. Currently, patients who are using *Mucuna* under medical advice generally report a lowering of their doses of conventional drugs, and fewer side effects, in both the short and long terms.

## 5. Contraindications and warnings

*Mucuna* has some drawbacks. In principle, the levodopa itself (albeit with other natural ingredients that improve tolerance) shares many of the contraindications and precautions applicable to synthetic levodopa. These warnings are well known, and we will review some of them.

I want to begin by highlighting the main stumbling block to the beneficial use of *Mucuna*: ignorance on the part of the patient and lack of medical information. A physician should monitor treatment at all times.

### 5.1. Patients do not know what they are taking

A major obstacle to treatment with *Mucuna* is that patients don't have clear ideas about the drugs' intended purpose. They have heard of several cases where *Mucuna* worked well, but usually these observations have come to them from people without any scientific knowledge, from nonprofessional websites or from commercial information intended for product sales.

*Mucuna* is sold freely on the Internet, and many patients take it without medical supervision. Worse still, they engage in speculation based on bizarre opinions they encounter in the forums, and they absorb this erroneous information and therefore lack sufficient knowledge to use it appropriately. However, occasionally patients are right or are very close to the truth, but there is still a danger of misuse. At times patients take *Mucuna* simply because despair leads them to try anything.

### 5.2. Most doctors are skeptics

Many patients complain of the disdainful reaction they encounter when they ask their doctors about adding *Mucuna* to their treatment regimen. As it is an "unorthodox" therapy, it is perfectly understandable that the physician does not want to prescribe *Mucuna*: it is not part of the generally accepted body of treatments they are trained to manage. When a doctor decides to incorporate *Mucuna*, he faces new difficulties, particularly with patients treated with other drugs. This requires the additional effort of studying the situation and designing a strategy for each individual case.

On the other hand, we cannot allow patients to treat themselves in hiding. Therefore, it is desirable that as doctors, we have to educate ourselves about *Mucuna* so that we can choose to use it or not in a particular type of patient. One should never despise the unfamiliar. After studying the properties of *Mucuna* and weighing its advantages and disadvantages, we should decide on a rational basis whether it is beneficial, neutral, or inadvisable for a specific case.

If the patient perceives that we master the subject, he will entrust his care to us, rather than attempting to treat himself. That way, he will cooperate if we ban the *Mucuna* or recommend a gradual dosage pattern. We earn their trust when we have enough information and credibility.



### 5.3. Why are there no frequent major problems?

*Mucuna* is not a placebo but, rather, has important effects. However anyone can buy it without a prescription, and most are taking it without medical supervision. These patients are not sufficiently familiar with the properties of *Mucuna*; they do not know the side effects or complications that may arise; they do not take into account the interactions with other medications or the differences between individuals.

While this scenario suggests a public health issue, it fortunately does not usually cause serious problems. Why? I think that one reason is the safety of the components of *Mucuna*, which has been used for millennia in thousands or hundreds of thousands of patients in India without significant harmful effects. Another issue is that the products are sold often in small doses as a dietary supplement. That is not, however, always the case: there are some preparations with excessive doses especially when combined with carbidopa (in Sinemet, Madopar, or Stalevo), dopamine agonists, or other antiparkinsonian drugs. It is necessary to use extreme caution.

### 5.4. Contraindications of levodopa

Although better tolerated, *Mucuna* contains a natural form of levodopa. In theory it should share the same contraindications, interactions, and precautions of synthetic levodopa: It is contraindicated in children, pregnancy, and lactation (prolactin inhibition) and schizophrenia or psychosis. It should be used with caution (and is best avoided) in cases of a medium to severe degree of heart disease or diabetes. Do not take it with MAOIs or with ergot. Use caution (due to the additive effect) if the patient takes levodopa (Sinemet, Madopar), COMT inhibitors (Entacapone Stalevo), or dopamine agonists (rotigotine, pramipexole, ropinirole).

### 5.5. Side effects with levodopa

*Mucuna* should not be used in individuals with known allergy or hypersensitivity to *Mucuna pruriens* or components. There have been some side effects of *Mucuna*. In a study of patients with Parkinson's disease, a derivative of *Mucuna pruriens* caused minor adverse effects, which were mainly gastrointestinal in nature. Isolated cases of acute toxic psychosis have been reported [51] probably due to levodopa content. Therefore, as with Sinemet and Madopar, its use should be avoided in patients with psychosis or schizophrenia.

### 5.6. Specific warning about *Mucuna*

We assume that all contraindications, interactions, precautions, and side effects that we know about synthetic levodopa should be considered when taking levodopa from *Mucuna*.

Specific contraindications include thinning of the blood (anticoagulants), and care should be taken with antiplatelet and anti-inflammatory drugs because *Mucuna* increases clotting time. *Mucuna* should not merge with anticoagulants (Sintrom, Dabigatran, heparin, warfarin) or with antiplatelet drugs such as clopidogrel. Caution should be exercised, and the additive effect should be taken into account if it is associated with acetylsalicylic acid and nonsteroidal anti-inflammatory drugs (NSAIDs).



We should also be careful with antidiabetic medicines: *Mucuna* lowers glycemic index, and thus is to be considered a potential additive effect. Other interactions are possible, so always consult your regular doctor. On the one hand, it can be argued that *Mucuna* has been used for many centuries in India and has been available for several years online without a prescription, and yet serious problems have not been revealed. But that is just an observation.

Regarding Sinemet and Madopar, we have thousands of controlled studies, while publications on *Mucuna* are still scarce. One must therefore use greater caution when choosing *Mucuna*. While the future appears to be positive, we need the confirmation of more scientific studies.

## 6. Dosage and presentations

To use *Mucuna* correctly, the premise is to be clear about what you want: it is simply a legume that contains levodopa naturally. Synthetic levodopa usually used in pharmaceutical preparations may be replaced in whole or in part by the levodopa contained in *Mucuna*.

This sounds simple, but the point is that the dosages and concentrations can vary, so the guidelines must be individualized, and as we said, at present the patients (and even some doctors) lack sufficient information.

### 6.1. Before using *Mucuna*

It is essential to find a neurologist who is interested in *Mucuna* and who is adequately informed about this amazing plant and how it can influence the treatment of Parkinson's disease. You should confirm everything with him and not conceal any information that may affect the treatment of your disease.

### 6.2. A strategy to start using *Mucuna*

First of all, ask your neurologist who knows your case. He can tell you if you can be treated with *Mucuna* or not, based on your specific situation, based on the stage of your Parkinson's disease, and taking account other pathologies and conditions.

Secondly, your doctor will advise you on the purchase of the adequate formulation of *Mucuna* depending on the dose administered. It is prudent to start with low-dose tablets and subsequently increase gradually; there is always time to increase the dosage. Patience is key in the beginning: if you rush treatment for quick results, it is likely that you will experience some side effects which, although they are usually mild, can be bothersome. If the treatment proceeds too slowly on the other hand, you may think that the *Mucuna* is not working and give up.

Third, adjustment of the treatment: you almost always have to modify the dose and frequently have to remove some of the drugs previously prescribed (for Parkinson's disease or for your other pathologies).

### 6.3. Careful with mistakes in dosage

There is no proven effective dose for *Mucuna*. In clinical studies, some patients take 15 to 30 grams (half an ounce to one ounce) of *Mucuna* preparation orally for a week, but I discourage such quantities, which I consider too high.

Any medication (which *Mucuna* is) should be administered initially in small amounts, keeping in mind the particular case of the patient and the purpose of the treatment. Doses of 15 and 30 grams of *Mucuna* seed extract were used for a specific experiment, with strict medical checkups, knowing well the formulation of the product and its origin and taking into account many other factors.

The researchers work under controlled conditions: they select patients without contraindications and remove any incompatible drugs and other medications that may alter the absorption or metabolism of levodopa, etc. That is not what happens when a patient buys *Mucuna* just anywhere and self-medicates with little information and without medical supervision.

### 6.4. Be careful when buying *Mucuna*

A consumer may purchase capsules of 200 mg of levodopa with a 15% concentration or 800 mg tablets with a 50% concentration, and these are two completely different products. Sometimes patients have bought the product on eBay knowing nothing of their provider, and they receive a package whose content is not guaranteed and whose concentration is not safe. The patient then will then dilute the material in water without knowing how much to measure out. Always use *Mucuna* extracts that are dispensed by known, reliable suppliers. In the final chapter, we give a brief description of some of these.

### 6.5. Presentations

They are so widely available that the Internet is flooded with numerous commercial offers. In summary the presentations of *Mucuna* may be grouped into seven sections: (1) powder; (2) tinctures or concentrated extracts; (3) low-dose (15 to 30 mg of “real” natural levodopa) capsules or tablets, ideal to start taking *Mucuna*; (4) medium- or (5) high-dose capsules or tablets, (6) tincture or *Mucuna* drops, and (7) *Mucuna* mixed with other substances.

The classic presentation of *Mucuna*, the only one used in clinical trials, is powder from *Mucuna* seeds. It is very bothersome to prepare as the powder must be diluted in water or other liquid (not milk because it hinders absorption). It has a very unpleasant taste that laboratories try to hide by sweetening it. The great advantage is the ability to adjust the exact for smaller doses that are always recommended at the beginning. In countries (such as Spain) where it is more difficult to find capsules or tablets with small doses, one may start with *Mucuna* powder. There are many brands offered, but here I describe only the original, which is sent directly from India.

### 6.6. Zanpora HP-200

This drug was marketed in India after the publication of an innovative study in Parkinson's disease patients in which an average of six sachets ( $\pm 3$ ) of *Mucuna* seed powder (7.5 grams with levodopa 250 mg, i.e., 3.3%) were administered to each patient.

I would like to emphasize that this *Mucuna* levodopa dose is relatively high (1500 milligrams), especially for those who had never taken levodopa, and if combined with one or two tablets of Sinemet, there is an obvious risk of overdose. Other than those patients, there were no problems probably because this natural levodopa is not combined with carbidopa (as in Sinemet). In theory the levodopa from *Mucuna*, as it lacks carbidopa, should be removed rapidly from the blood, unless the plant contains other ingredients to avoid it.

After taking the *Mucuna* powder (dissolved in water), blood levels of levodopa behave similarly to those observed with the synthetic version of levodopa. The difference is that the maximum dose does not show as marked an effect [45] and clinical efficacy is similar or greater.

### 6.7. Common mistakes in prescribing Zandopa

Equivalences of Zandopa powder are administered to people who take only levodopa (without carbidopa), something which hardly occurs in the West, so that errors are very common.

According to the manufacturer, every measure of *Mucuna* powder (7.5 grams) is equivalent to 250 mg of synthetic levodopa. But this is only when the patient does not take carbidopa at all. However, almost all patients mix *Mucuna* powder with some Sinemet or Stalevo in which case it is necessary to assume that the carbidopa is working.

The equivalence for Zandopa is not clear to the uninitiated. If you follow the laboratory indications, you must give 30 grams of powder to replace the Sinemet 25/250 tablet (four small cups). This is the ratio that was used in the original study, but in practice it is too high and can cause side effects (nausea, vomiting, and malaise) so I do not recommend it. The dosage is individualized, and you have to start with small, adequately spaced doses. The laboratory has verified this and thus expressed it in the brochure, although not sufficiently emphasized.

## 7. *Mucuna* and conventional levodopa

*Mucuna* preparations usually sold online contain small amounts of levodopa. Furthermore, it is not combined with (carbidopa-like) “enhancers” and so has hardly any effect on symptoms.

As previously stated, in order to achieve the clinical effect of a tablet of Madopar or Sinemet, 1000 mg of levodopa *Mucuna* must be given. That would be like 4 scoops (30 g of seed powder) of Zandopa or nearly 17 capsules of other preparations providing 60 mg per dose. For example, a patient taking four daily tablets of Sinemet or Madopar who wants to switch to *Mucuna* alone would need 4000 mg natural levodopa daily, i.e., 120 mg of seed powder (a bottle of Zandopa contains 175 mg) or 66 capsules of Bonusan (60 mg levodopa each) or 40 capsules of Solbia (100 mg levodopa each). Few patients want to take on such a cost.

The problem is further complicated by the fact that the actual content of levodopa in many products sold online is lower than stated on the label [52].

### 7.1. Adding carbidopa to *Mucuna*

The synthetic levodopa in Sinemet is enhanced by carbidopa. This increases its clinical effectiveness and prevents peripheral side effects (nausea, tachycardia).

Carbidopa further improves the effects of *Mucuna*: it reduces the mild side effects and doubles or triples its effectiveness. This factor must be taken into account when a patient combines *Mucuna* and Sinemet (or Madopar or Stalevo): the carbidopa in these drugs also interacts with the natural levodopa in *Mucuna* by strengthening its clinical effects, and the dose should be greatly reduced.

And what happens when the patient does not take Sinemet or other drugs? Then *Mucuna* may be insufficient. These patients complain that *Mucuna* “does not do anything,” and this is due to the fact that their decarboxylase is quickly removed from the blood, without allowing time for a sufficient amount to reach the brain.

The solution seems to be to add carbidopa, which in some countries is sold separately (as Lodosyn). When Lodosyn is not available, there is the option of taking half a tablet of Sinemet Plus (12.5 mg carbidopa) and subtract the amount of synthetic levodopa (50 mg), taking into account that it will now be more potent.

### 7.2. Enhancing levodopa

One inexpensive and clinically effective option is to use levodopa enhancers that are contained in conventional drugs. It is a good idea to mix the *Mucuna* seed powder with very low doses of Madopar (e.g., half a tablet in the morning and half at night). Thus, only 200 mg of synthetic levodopa is provided, but this has the advantage that there are 50 mg of benserazide included. This will greatly enhance the effectiveness of natural levodopa in the added *Mucuna*.

One can also add green tea; its polyphenols are inhibitors of decarboxylase (such as benserazide or carbidopa), further reinforcing the levodopa. The overall bioavailability of levodopa will be improved. In some patients a spectacular result has been obtained, as we have previously published [53, 54].

### 7.3. Risks of combining *Mucuna* and green tea

Green tea enhances the effect of beans in general and of *Mucuna* in particular. This effect can also be seen in patients taking Sinemet or Madopar: it is recommended that patients be aware of this phenomenon due to the increase in potency it can produce.

*Carbidopa-like effect.* There is something in green tea that acts like carbidopa. It contains polyphenols which inhibit dopa-decarboxylase [55], an action similar to that carried out by the carbidopa or benserazide contained in Sinemet or Madopar.

*Entacapone-like effect.* In addition, there is something that acts like entacapone in green tea. Polyphenol, epigallocatechin gallate (EGCG) promotes the entry into the brain of levodopa and prolongs its bioavailability in the bloodstream because it inhibits the COMT enzyme [56]. This action is similar to that of entacapone, namely, that beans mixed with green tea have Stalevo-like effects but with different proportions. Obviously, if you take levodopa (*Mucuna*

or otherwise), its effectiveness will be reinforced, and this should be taken into account as there is risk of overdose. Always consult your doctor.

These “carbidopa-like” and “entacapone-like” effects can be seen with green tea, and they are independent of their other neuroprotective benefits [57] so the tea is recommended for many Parkinson's disease patients.

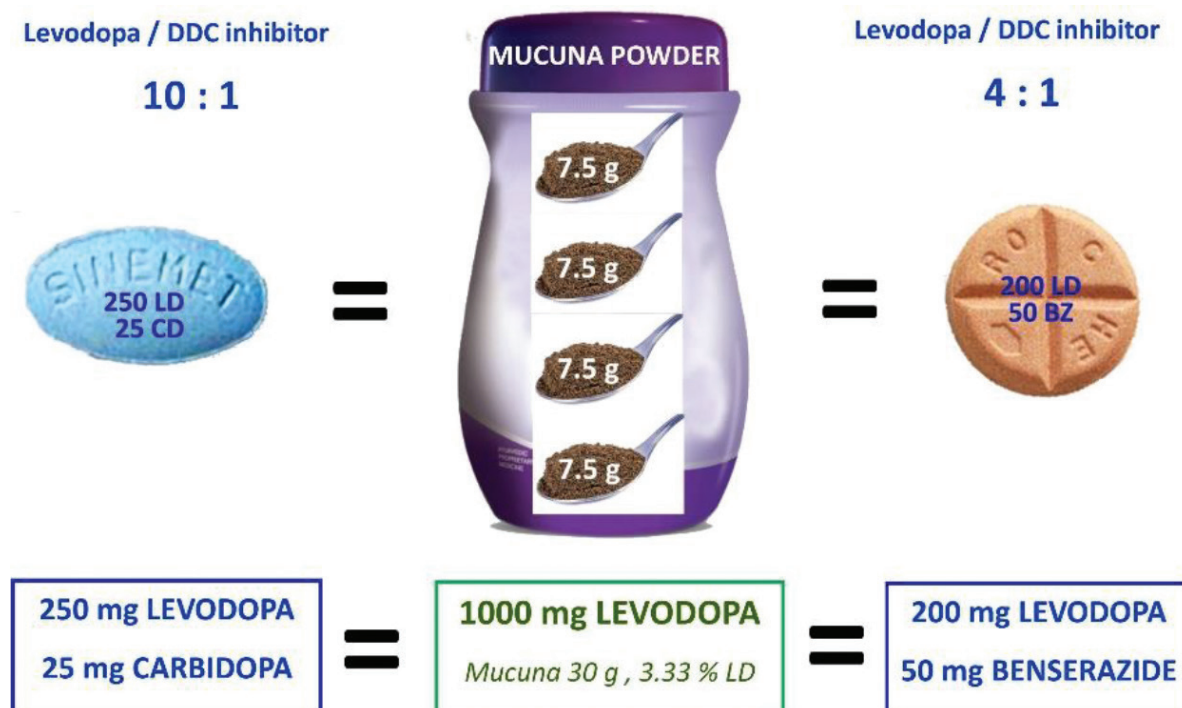
#### 7.4. Complexities of adjusting *Mucuna*

As *Mucuna* seed powder does not contain carbidopa (theoretically), the clinical effectiveness of 1000 mg of natural is equivalent to a tablet of Sinemet 250/25 or of Madopar 200/50 (**Figure 1**).

#### 7.5. *Mucuna*: the levodopa for the poor

In Africa and the Caribbean, I have seen Parkinson's disease patients in a very deteriorated state, who are not treated with levodopa because they are unable to afford Sinemet, Madopar, or Stalevo. Neither they nor their governments can bear this expense. Ironically in their countries, levodopa is everywhere; *Mucuna* grows spontaneously and spreads so fast that they even have to pull up it so it does not invade other crops.

The plant contains a large amount of levodopa, a treasure trove for those patients in the third world. Ailing inhabitants need this levodopa to live better and longer. It is outrageously unfair. A recent study [58] offered an option: the use of *Mucuna* levodopa is very accessible in countries that cannot afford Sinemet, Madopar, or Stalevo.



**Figure 1.** Clinical effectiveness of *Mucuna* compared with Sinemet and Madopar [54] (see text).



## 7.6. Neurologists in Ghana and Zambia

I applaud the laudable deeds of neurologists who have opened clinics for patients in Ghana and Zambia where they have already served over 100 patients. There they cannot prescribe Sinemet because it costs a prohibitive dollar and a half each day per patient; meanwhile *Mucuna pruriens* grows spontaneously all around them. With the collaboration of the local authorities, they began to systematically prepare seeds of *Mucuna* (harvesting 12 different types) cooking them first to eliminate antinutritive substances.

They administered *Mucuna* without special extraction methods, although they could not integrate carbidopa, and have obtained the first results: the levels of levodopa in the blood increase, demonstrating that it is being absorbed [58, 59]. Patients improved although the system is so primitive that they suffered some side effects such as nausea, dry mouth, and orthostatic hypotension [59].

The initiative of these pioneers of *Mucuna* treatment in Africa is promising. However, this situation must be regulated. Who could ever infringe on such an important humanitarian effort?

Studies of *Mucuna* in Parkinson's disease should be expanded. Inexpensive levodopa should be provided to patients with few resources in poor countries. It could be that doctors and patients of the West finally imitate the less fortunate.

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