Levodopa and Medicinal Beans

In the fall of 2005, on the PLWP2 (people living with PD) website, Peter Fox wrote about beans that contain levodopa. This was the first I had heard of it and I was delighted. It meant I could, if I chose, grow my own medication. The beans with levodopa are fava beans (broad beans), which will be easy for me to grow, and a tropical bean called mucuna, which will be more of a challenge. When I looked into the possibility of using these beans as medication, I soon realized it wouldn't just be a matter of adding them to my diet. There are considerations of timing and levodopa strength and the complication that levodopa is usually taken in conjuction with other drugs.

Levodopa (L-dopa) is the medicine of choice for relieving PD symptoms. This is because levodopa is a precursor for dopamine, the chemical messenger that is in short supply in PD. There are dopaminergic neurons, both in the brain and in other parts of the body, which manufacture, store and regulate the release of dopamine. In PD, the neurons of the substantia nigra have decreased in number to where they are unable to manufacture an adequate supply of dopamine. In the early stages of PD, levodopa medication relieves most, but not all, PD symptoms and does this with minimal side effects.

As PD progresses, with a further decrease in the number of dopaminergic neurons, dyskinesia becomes a common side effect of levodopa medication. Dyskinesia (random muscle contractions) occurs when the supply of dopamine from levodopa medication swamps the neurons, exceeding their ability to regulate the release of this chemical messenger.

There is no general agreement about when levodopa medication should begin. Some doctors recommend putting off the use of levodopa as long as possible. They feel that levodopa stresses our neurons which, in turn, leads to dyskinesia. By delaying until we really need it, we delay the onset of dyskinesia.

An alternate theory about levodopa use is that dyskinesia has nothing to do with the length of time that levodopa has been used. Rather it is purely a function of the number of remaining neurons, so we might as well start taking levodopa in the early stages of PD.

In fact, levodopa medication, by relieving the remaining dopaminergic neurons of one of their tasks (the production of dopamine), may slow the loss of neurons. This possibility received qualified support from a study done by Fahn et al called *Levodopa and the progression of Parkinson's disease* (N Eng J Med, 2004 Dec 9; 351(24): 2498-508). 361 patients with early PD were given levodopa (small, medium or large doses) or a placebo, with nobody knowing who was getting what. After 40 weeks, medication was stopped for two weeks and then standard movement tests were used to evaluate PD progress. The placebo group had the worst scores; the large dose levodopa group had the best scores. This would be a clear vote for early levodopa medication if the experimenters had not also done a new analytical test called neuroimaging which showed maximum PD progression for the large dose levodopa. In other words, the opposite result. Because neuroimaging is new, the experimenters were inclined to place more credence on the movement tests. But the contradictory results made them somewhat tentative in their conclusions.

Levodopa is not usually the first medication prescribed for PD. Dopamine agonists make message receptors more sensitive to chemical messengers, with the result that a smaller amount of dopamine is sufficient to transmit the message. Most neurologists start off new patients with a dopamine agonist and introduce levodopa later (the patient typically continues to take the dopamine agonist).

Dopamine, itself, cannot be taken as a drug for PD because it is unable to cross the blood brain barrier (BBB). The dopamine precursor, levodopa, can't cross the BBB either; at least, not on its own. But there are amino acid transporters that hang out at the BBB (like Charon at the river Styx) which are willing and able to ferry levodopa across. Willing, that is, unless you have eaten a protein rich meal at the same time as swallowing your pill. Then levodopa will have to compete with other amino acids for the services of the ferry. Once across the BBB, there are enzymes waiting which convert levodopa into dopamine.

But that's not the whole story: the enzymes which greet levodopa as it enters the brain have some identical twins in the bloodstream outside the brain. Levodopa which gets converted to dopamine in the peripheral bloodstream (that is, outside the brain) is of no use to the brain. The presence of these enzymes in the peripheral system means that for every molecule of levodopa that makes it to the BBB unchanged, there are many more that get converted to dopamine and get turned away. This creates a problem. You have to take a whack of levodopa in order for a sufficient dose to enter the brain. And then there's all that excess dopamine in the peripheral bloodstream looking for a home. Some of it can be used by your kidney; some can be used for regulating blood flow. The rest will cause nausea, vomiting and general unpleasantness.

Enter carbidopa. It acts as a bodyguard for levodopa, keeping enzymes at arms length. It does this well enough to allow five times as much levodopa to reach the brain. At the BBB, carbidopa gets turned away. This is convenient because once levodopa enters the brain we don't want carbidopa present to protect levodopa from the enzymes which will convert it to dopamine. When levodopa and carbidopa are taken together, a much higher percent of the levodopa reaches the rain. So the amount of levodopa taken can be reduced accordingly; this, in turn, prevents side effects by reducing the amount of excess dopamine in the peripheral bloodstream.

All levodopa pills come with enough carbidopa (or a similar drug) to protect the levodopa during its trip through our digestive system and bloodstream to the brain. Carbidopa is never 100% effective in its bodyguard action but it makes a big difference in the amount of levodopa that makes it to the brain.

Fava and mucuna beans do not appear to contain anything corresponding to carbidopa. From a medicinal point of view, the lack of carbidopa in the beans creates a problem. For an adequate dose of levodopa to reach the brain, a lot of beans have to be eaten. This is unhealthy, both because of the large amount of levodopa that gets converted to dopamine in the peripheral system and because beans typically contain small amounts of toxins. Bean toxins don't cause any difficulty if the beans are just eaten occasionally or in small amounts. But frequent meals of large helpings of beans would not be healthy.

In the USA, carbidopa is available by itself (under the trade name Lodosyn). Because it is a specialty item, it costs twice as much as a levodopa pill which has the same amount of carbidopa plus the levodopa. In Canada, Lodosyn is not an approved drug. So taking a Lodosyn pill with a small helping of beans is not an option.

At present, I have a prescription for 25 mg Carbidopa/ 100 mg Levodopa. Sometimes I just take the pill. But whenever convenient, which is most of the time, I break a pill in half and eat enough fava bean sprouts or mucuna bean powder to provide the other 50 mg levodopa. My assumption is that the bean levodopa will be able to piggy back on the carbidopa from the pill. Also, I know I am getting 50 mg levodopa from the pill so if my estimate of the levodopa content of the beans is a little off, the total error is less than it would be if I relied entirely on the beans. So far, this is working very well. But I'm in the early stages of PD and my system is more adaptable than it will be 10 years from now.

Vicia Faba and Mucuna Pruriens

These two bean species are the only plants known to contain significant amounts of levodopa. Despite

having this in common, they are quite different in the way they distribute it. In fava, the seeds are the plant part with the least amount of levodopa (0.2% or less). In mucuna, the seeds are the plant part with the most levodopa (2.0% to 9.0%).

Leaves, stems, pods and blossoms of fava have 10 times more levodopa than seeds. The plant parts of mucuna have less than one tenth as much levodopa as the seeds. This affects the way we use these beans.

Mucuna has a long history of medicinal use in India where it was used to treat parkinsonian symptoms long before Dr. Parkinson gave his name to PD. The seeds are made into a powder which usually has about 4% levodopa.

Two similar clinical studies have been done with mucuna powder in place of carbidopa/levidopa pills. They are Manyam et al, *An Alternative Medicine Treatment for Parkinson's Disease: Results of a Multicenter Clinical Trial* (J of Alternative and Complimentary Med, 1995, Vol 1, No 3, p.249-55) and Katzenschlager et al, *Mucuna Pruriens in Parkinson's Disease: a double blind clinical and pharmacological study* (J Neurol Neurosurg Psychiatry 2004; 75: p.1672-1677). The patients in both studies did as well or better on mucuna powder as on carbidopa/levodopa pills This is remarkable to me because in order to have an effective dose of levodopa reach the brain (without the aid of carbidopa) the quantity of levodopa in the powder was five times what would have been given in a pill; and therefore there was much more excess dopamine in the bloodstream with the concommitant disposal problem.

Despite the success of mucuna powder in these tests, I am concerned about possible problems with consuming a large amount of bean powder on a long term basis. Katzenburger speculates that "it might be appropriate to administer mucuna preparation in combination with a peripheral dopa decarboxylase inhibitor [carbidopa] which may further improve tolerability and efficacy." This is the approach which, it seems to me, holds the most promise. So far, rats have been the main beneficiaries.

When mucuna was tested in conjunction with carbidopa, using rats (with induced parkinsonism), the results were quite impressive. This test was by Hussian et al. Their report was called *Mucuna pruriens proves more effective than l-DOPA in Parkinson's disease animal model* (Phytotherapy Research, 1998, Vol 11, Issue 6, p 419-423).

They gave carbidopa to the rats along with the mucuna to see if carbidopa has the same beneficial effect on mucuna derived levodopa as carbidopa has on manufactured levodopa. It did. In fact, carbidopa may have worked even better with the levodopa from mucuna than with levodopa in a pill. When the rats were put through some standard movement tests after being given equal amounts of levodopa, either manufactured or from mucuna, the rats who got the mucuna did better on the tests. Then the experimenters reduced the quantity of mucuna and found that half as much levodopa from mucuna produced the same benefit as a full measure of manufactured levodopa.

Their conclusion: "This study suggests that mucuna may contain unidentified antiparkinsonian compounds in addition to l-DOPA, or it may have adjuvants that enhance the efficacy of l-DOPA."

The combination of mucuna and carbidopa worked so well with rats that a similar trial with human subjects seems inevitable. If one exists, I have been unable to find it. The closest I have come is a mini-study in Turkey where PD patients ate fresh cooked favas in addition to their usual PD medication. Apaydin et al called their report *Broad bean (Vicia faba)-A natural source of L-dopa-Prolongs "on" periods in patients with Parkinson's disease who have "on-off" fluctuations* (Movement Disorders, 2001, Vol 15, Issue 1, p164-166).

Doctors at a clinic in Turkey received reports from their PD patients that when they ate favas in addition to

their medication, they felt better. So the doctors recruited three patients willing to eat 250 gram portions (fresh cooked whole pods) on a regular basis, and to keep a detailed diary.

They were to continue on their usual carbidopa/levodopa medication so they had carbidopa in their system to guard the fava ingredients as well as to protect the levodopa in the pill.

Their conclusions: "We observed a beneficial effect of *Vicia faba* in our patients manifested by strikingly prolonged “on” time and shortened “off” time. We were surprised by the reported magnitude of our patients’ responses, given the fact that previous trials of higher doses of carbidopa/levodopa seemed to provide no further benefit. These observations are not readily explained by assuming that broad beans are simply a source of levodopa. For example, patient no. 2 was able to experience a sustained response from broad bean meals ingested on alternate days. Also, somewhat surprisingly, patient no. 3 experienced decreased dyskinesias with the addition of broad bean supplementation and reduction of carbidopa/levodopa therapy. This patient had previously failed to respond satisfactorily to carbidopa/levodopa adjustments which should have accomplished the same result if this was simply a levodopa effect."

"A placebo effect may have contributed in this unblinded trial, but the magnitude of the reported responses raises the possibility of other mechanisms. For example, the amino acid milieu generated from broad bean administration may favor the selective transport of levodopa across the blood–brain barrier. Alternatively, other products derived from broad bean may complement the antiparkinsonian effect. These results suggest that a controlled trial with close monitoring of the clinical response is warranted."

Some of the Turkish patients reported they did not get the same benefit when they cooked with dry beans. This might be due to the low levodopa content of dry fava beans. Or it might be that the cooking, which is usually much longer for dry beans than for fresh green beans, further degraded the small amount of levodopa in the beans.

This argues for growing your own fava beans and eating them as a green vegetable. Not so with mucuna. Since the dry bean is the best source of levodopa from mucuna, buying powder from a commercial source may as good as growing one's own. Especially considering the hardness of the seeds. I doubt that anything short of an industrial grinder would be able to turn these seeds into powder. When I got a few seeds for growing in my greenhouse, I tried soaking the seeds prior to planting. Not a drop penetrated the seed coat. So I tried scoring the seed coat with a sharp knife — it didn't make a mark. I got out my hacksaw, held the seed firmly with a pair of pliers, and made a light pass with the saw — I didn't want to damage the kernel — I needn't have worried — still no mark —this seed coat was roughly the same hardness as stainless steel. I got more aggressive with the saw and was able to cut through the seed coat. The seeds then took up water quite readily.

I will try growing mucuna but do not envision making my own powder, even if I am successful in growing the beans. A source for mucuna powder is:

> Garry & Sun
> 550 E Plumb Lane,Suite 301/306
> Reno, Nevada 89502
> Website: Garry and Sun Natural Remedies

They import it from India where it is called kaunch powder.

One level teaspoon powder weighs 2.5 grams. Assuming 4% levodopa, that works out to 100 mg levodopa per teaspoon. How to deal with the powder? It is nearly tasteless so ½ teaspoon sprinkled on the peanut butter in a sandwich does not affect the flavour. If butter is softened, but not melted, mucuna powder will

blend easily into the butter which can then be spread on bread, toast, biscuit. Levodopa is heat sensitive, so cooking with the powder is not recommended (when mucuna is being used as a food by regular folk, they cook the beans at some length to get rid of the levodopa).

Convenience is one of the main advantages of pills versus beans. Just remembering when to take medication is hard enough by itself. When that time comes it will, more often than not, be inconvenient to cook up some beans or measure out some mucuna powder, mix with butter and spread it on a slice of bread. One way around this is to mix powder with something edible ahead of time and have it divided into pieces with known amounts of levodopa.

If you are looking for a way to justify eating chocolate, heat a package of bakers chocolate just enough to make it soft. While the chocolate is warming up, blend 25 g (just over 3 tablespoons) mucuna powder into 2 tablespoons of soft butter. Blend this thoroughly into the soft chocolate until there is no colour variation. Spread on wax paper and, when it cools, cut into 20 equal pieces. Each piece will have roughly 50 mg levodopa.

I do something similar with Rice Krispie squares. This is a slightly altered version of the recipe which comes on every box of Rice Krispies:

- 1/2 cup butter
- 1/2 lb (225 g) mini marshmallows
- 3/8 cup (6 tblsp) mucuna powder
- 6 cups Rice Krispies

Note the doubling of the amount of butter — half goes with the melting marshmallows as usual (in a large pan on the lowest heat, stirred frequently); the other half is softened and blended into the mucuna powder. When the marshmallows have melted, stir in the butter-powder paste (quickly but thoroughly). Then stir in the (previously measured out) Rice Krispies. Spread out on wax paper and cut into the 30 equal pieces to give about 60 mg levodopa per square.

If you are going to experiment with mucuna powder, I recommend getting half your levodopa dose from a carbidopa/levodopa pill and half from the mucuna powder. My neurologist is okay with this, for me, but you should get the blessing of your own neurologist.

Levodopa in mucuna powder loses strength over time and it won't come with a strength rating, so you will not know, with any degree of precision, how much levodopa you are getting from the mucuna powder. However, one of the things I learned from reading the PLWP2 discussion board is that people with PD are remarkably well tuned in to their medication. After a few doses you will probably be able to judge (better than any measuring device) whether you should adjust the dose.

Fava beans are not quite so easy to deal with as mucuna, though there are many more options with fava. A warning note first. Before giving serious consideration to fava beans, find out if you have the genetically based problem called favism. This can be deadly if you have it and ignore it.

Favism is a hereditary abnormality in the activity of a red blood cell enzyme. This enzyme, glucose-6-phosphate dehydrogenase (G-6-PD), is essential for assuring a normal life span for red blood cells. This enzyme deficiency may provoke the sudden destruction of red blood cells and lead to hemolytic anemia with jaundice following the intake of fava beans. You can determine whether you are G-6-PD deficient by a simple blood test.

Assuming you get the green light for fava beans, the easiest form of the bean to obtain from commercial sources is the dry bean. I have eaten a few dry fava beans and found the mild nutty flavour quite agreeable.

I don't recommend this, however — dry beans are quite hard and eating them this way would almost certainly lead to broken teeth. Also, they are low in levodopa so a powder made from them would be the least attractive option.

Fava beans come in two general types. The "major" vegetable type (also called broad bean), with a flat seed like a lima, is usually grown for fresh eating; tends to be large seeded, but not always. The "minor" field crop type (also called horsebean or ticbean), with a round seed like a chick pea, is more often grown for use as stock feed and for cooking from the dry bean.

Fava beans, like all beans, are rich in the amino acids phenylalanine and tyrosine which are precursors of levodopa. In the body, phenylalanine is converted into tyrosine. Tyrosine in turn is converted into levodopa, norepinephrine, and epinephrine, three key neurotransmitters. Tyrosine hydoxylase is the enzyme which converts tyrosine to levodopa.

It would appear that what distinguishes fava from other beans is that fava has a genetic blueprint for tyrosine hydroxylase. Because as soon as the bean seed starts to grow, levodopa content increases — presumably from the action of tyrosine hydroxylase on tyrosine.

One way to use dry beans of the minor type is to sprout them. Sprouting increases the levodopa content of the bean by a factor of five. My rule of thumb is that each sprouted fava bean contains two mg levodopa. The seed coat of a sprouted fava is rubbery and tasteless with negligible levodopa. When I am not rushed in the morning, I start my day with a half tablet of 25/100 carbidopa/levodopa plus 20 to 30 fava sprouts which I skin as I go.

While a powder from seeds is very low in levodopa, the dry seed is not the only potential source of powders. Simon de Boer, an organic farmer in South-Western Ontario, grew a field of favas and made powders from green leaves and pods dried in a low temperature dehydrator. Levodopa content of these powders is 1% to 2%. They can be used in the same way as mucuna powders.

Canned fava products are low in levodopa and of little interest, from a medicinal point of view.

Fresh green immature pods are one of the best sources of levodopa in fava. These are available from time to time from green grocers. The pod shell is much higher in levodopa than the green beans inside so edible pod varieties are best from a medicinal point of view. The trick with these pods is to not cook them any more than necessary and to eat them right away. Pods steamed for 15-20 minutes just lose 10% of their levodopa content. If set to one side and kept warm or allowed to cool slowly, they lose much of the remaining 90%.

Measuring Levodopa

When I grow 30 different varieties of fava in the summer of 2006, in addition to evaluating for flavour, I will be looking for the varieties highest in levodopa. To do this, I will have to measure levodopa content. I've been working on a kitchen chemistry method of measuring levodopa. This project has been a mixture of fun and frustration. So far, I have been able to determine the relative strengths of similar samples. That is, I can determine with confidence which fava seeds have the highest levodopa content. But when comparing fava seeds with fava pods or mucuna powders or with a standard 100 mg pill, it is harder to get repeatable results.

A kitchen chemistry method should be low tech and use chemicals which are not dangerous. The key chemical in this case is potassium iodate which under certain circumstances can be explosive. So it has to be handled with respect. Nevertheless, it is the form of iodine used in iodized salt, so if trace amounts got into our food, it would be more likely to do us good than to do us harm.

Levodopa reacts with potassium iodate, at pH 5, to form a reddish-orange compound. The intensity of the colour can be used to measure the amount of levodopa. When two samples are being compared, the one which is more intensely coloured is diluted until it is visually the same as the weaker one. The amount of dilution is used to calculate the relative strengths of the two samples. Relying on a visual determination of equal colour is less accurate than measuring with a spectrophotometer, but you can get surprisingly close when doing a visual comparison. The most significant errors with this method come from other factors.

A benefit from wrestling with the measuring problems is a better understanding of bean chemistry. The main difficulty I have encountered is that different sample types produce different shades of orange. Fava seeds produce a brownish orange, fava sprouts and pods are reddish orange, mucuna powder is a different shade of reddish orange and manufactured levodopa is yellow orange (though, with time, it gets more and more reddish). This makes comparing colour intensity very difficult. It also raises the question of what is being measured. Is it all levodopa? Does some of the colour come from chemical compounds which are closely related and biologically active in the same way as levodopa? Or is some of the colour coming from compounds which are unrelated to levodopa?

To answer this latter question, I checked a few other bean species and got no significant colour from them. This gives me confidence that any colour I get is probably from chemicals closely related to levodopa. Nevertheless, assigning a strength value is still difficult.

Another problem is that the colour shade and intensity are time dependent. The colour gradually becomes more intense and the colour shade gradually moves from yellow to red. To some degree this can be solved by measuring at a specific time after iodate addition.

Colour is also affected by pH. At first I tried adjusting pH using citric acid and pH paper. This worked reasonably well but required care and good judgement. And dilution changed the pH. I eventually settled on using a buffer.

There is also the problem of sample preparation so that all of the levodopa in the sample is dissolved and measured. In particular, if seeds are ground up for measuring purposes, there tends to be some variation in particle size; and seed chunks (as compared with fine powder) will be much slower to release their levodopa content into solution. Also, the prepared sample has to be filtered and any haze in the final sample interferes with strength determination.

The net result is a fairly large potential error in strength determinations. Probably on the order of 25%. In other words, if I measure a mucuna powder at 4%, it could be as high as 5% or as low as 3% — a huge error range from a scientific point of view; but these rough measurements still provide a useful guide for deciding how much to take as PD medication.

Return to Ken Allan's Homepage