Chronicle of a Parkinson's-Patient Researcher

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This is the first article in a chronicle of research subjects being explored by a retired research scientist (chemist, physicist) diagnosed with Parkinson's disease in 2018. It is my way of sharing what I learn about Parkinson's disease by reading research papers published by experts with the aim of helping control the progression of my own Parkinson's disease and for the benefit of others. I will try to explain the science involved and how PwP can use dietary changes or supplements to try to slow the disease. Any observations that I report here, unless otherwise indicated apply only to me and to my type of Parkinson's disease. I attach equal importance to negative observations as to positive ones. Be aware that although I am an experienced researcher, I am a beginner in these fields and I don't have the support of a professional team to question or discuss any misinterpretations I may make. I have made mistakes already and I will make others, but I'm happy to do that to learn more about this disease. My hope is that other scientists and PwP will read, criticise or pick up on some points raised here and continue the research effort.

Observations of the impact of dietary isothiocyanates on Parkinson's disease symptoms. Activating the Nrf2 transcription factor to combat oxidative stress.

Abstract *Up-regulating the Nrf2 transcription factor as a means of increasing the expression of antioxidant and anti-inflammatory genes directly inside neurons has long been proposed as a promising method of combatting oxidative stress and associated inflammation in neurodegenerative diseases. This paper covers the reasoning and methods adopted by a Parkinson's patient leading to the use of a natural Nrf2 inducer, an isothiocyanate extracted from Brassica seeds to explore this phenomenon. It documents my personal observations over 5 months in terms of the evolution of my symptoms. No attempt is made claim scientific proof or otherwise for any hypothesis. These observations are simply presented as a personal record to encourage reflection and more controlled experimentation with dietary isothiocyanates.*

Introduction

It is well accepted that up to 70% of neurons that produce the neurotransmitter dopamine are damaged or already dead at the moment of diagnosis of Parkinson's disease [1]. What causes this cellular damage and decline? Accumulating evidence extensively reviewed [2, 3] indicates that much of this cell damage can be ascribed to a cascade of three events operating in a vicious circle:

- Oxidative stress in neurons: the excessive presence of free radicals, H_2O_2, peroxides etc. that cause oxidative damage to cell membranes and mitochondria,
- Chronic inflammation of neurons induced by oxidative stress that prevents neurons from healing and is a major cause of neurological pain.
- Excessive damage to mitochondria (organelles in cells that generate energy) leads to reduced cellular energy production and more oxidative stress. This loss of cellular energy production may be a major cause of fatigue felt by patients.

A large survey of the dietary habits of Parkinson patients [4] demonstrated that the typical low-calorie Mediterranean diet, rich in polyphenols and omega-3 oils, fresh fruit, fresh vegetables, nuts, fish, olive oil and red wine is associated with a slower progression of Parkinson's disease, compared to a high-calorie western diet, based on red meat, fried foods, soft drinks and highly processed

foods. Such an antioxidant diet does not however appear to be able to break the vicious circle described above and stop disease progression altogether. To do this we may also have to reactivate a genetic process that operates well when we are young but slows down with age. This process is called the Nrf2/ARE pathway. The good news is that we can reactivate it with dietary isothiocyanates.

Oxidative stress is believed to be due to the failure of the internal system to fully control the level of oxidative molecules in brain cells. This system is controlled by a gene transcription promoter sequence called the Antioxidant Response Element (ARE). As we grow older, the activity of ARE declines leading to a higher oxidative imbalance, cellular damage, inflammation and reduced cellular function [5, 6]. Let us take a look at the mechanism that controls the Nrf2/ARE pathway. It's not really that complicated once you get used to the names.

The scientific case for up-regulating the transcription factor Nrf2

NFE2L2 is a gene situated on human chromosome 2 which expresses a protein known as the transcription factor Nrf2.

Under stable conditions, the transcription factor Nrf2 is held in the cytoplasm of cells on docking sites called Keap1. It's half-life is rather short (15-20 min) after which it is degraded and new protein must be synthesised. When stimulated by oxidants, indirect anti-oxidants or reactive oxygen species (ROS), Keap1 loses its ability to target Nrf2 for degradation which then migrates into the nucleus and binds to the enhancer sequence ARE. Whenever Nrf2 is bound to ARE, induction continues to promote the production of antioxidant enzymes, anti-inflammatory cytokines and to suppress inflammatory cytokines. The degree of induction of ARE depends on the quantity of Nrf2 present in the nucleus. With advancing age, the activity of Nrf2 declines and oxidative stress increases.

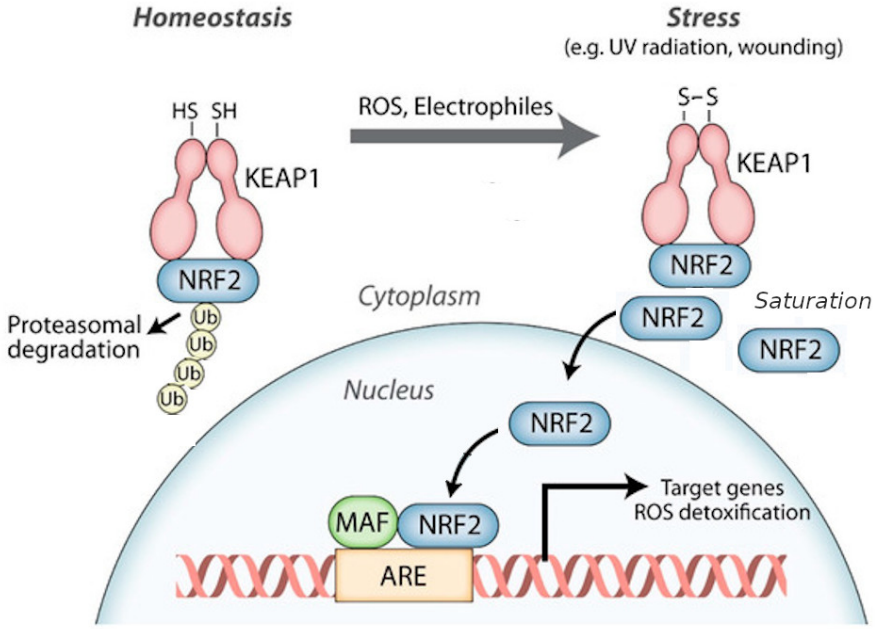


Fig. 1. Nrf2 protein is normally held in docking sites of the protein Keap1 in the cytoplasm and is subsequently degraded. When Keap1 is activated (oxidised) by ROS or by indirect antioxidants, Nrf2 is no longer degraded but saturates the Keap1 site. Newly synthesised Nrf2 then accumulates in the cytoplasm and migrates to the nucleus where it forms a hetero-dimer with MAF and binds to the gene promoter sequence ARE. This promotes the transcription of a battery of antioxidant and anti-inflammatory genes. Illustration adapted from P. Hiebert and S Werner. [7]

ARE are enhancer sequences found in the promoter regions of a battery of genes encoding antioxidant and detoxifying enzymes and cytoprotective proteins. When activated, they induce the transcription of genes that lead to the expression of antioxidant enzymes anti-inflammatory cytokines and to the suppression of inflammatory cytokines. Cytokines are small messenger proteins that generate or suppress inflammation. ARE induction has the capacity to break the vicious circle of oxidative stress, inflammation and mitochondrial damage in brain cells.

Keap1 is therefore a negative regulator of the Nrf2 pathway. One way to up-regulate Nrf2 is to disactivate Keap1. This can be done using indirect antioxidants such as dietary isothiocyanates extracted from seeds of the cruciferous vegetables that include broccoli, cabbage, turnips, brussels sprouts and mustard. Research on this has been ongoing for 20 years. It is one of the main reasons why broccoli is recommended as a health-promoting food. Sadly, the quantity of isothiocyanate in vegetable broccoli is much too small to have any significant effect on Parkinson's disease.

in 2009, a team lead by Dr Antonio Cuadrado, a leading neuroscience researcher in Madrid, turned to the induction of the gene transcription promoter sequence termed Antioxidant Response Element (ARE) by up-regulating the transcription factor Nrf2 as a way to stimulate the production of endogenous antioxidant enzymes and anti-inflammatory cytokines directly inside each cell. They were able to demonstrate the protective effect of the induction of ARE on Parkinson's disease in animal models thanks to a project funded by the Michael J. Fox Foundation (MJFF). Then, in collaboration with Prof. Paul Talalay, the discoverer of the natural isothiocyanate, sulforaphane, they applied for a new grant from the MJFF for a phase 2 clinical trial. The study, called RASTOP (Rasagilin And Sulforaphane Therapy for Parkinsonism), was supported by 16 hospitals in several EU countries.

> **"This trial was not funded. The argument given was that in the case that it would show a relevant efficacy, no company would be interested in covering the huge expense of a phase 3 trial for a natural compound that could not be patented" (*A. Cuadrado, private communication*).**

This statement is a damning indictment of the situation in which Parkinson's patients and researchers find themselves. A potential life-changing remedy for Parkinson's disease patients, backed up by outstanding research, has been blocked for years, not because of possible doubt about it's efficacy, but because the natural product proposed could not be patented. Research has nevertheless continued to make progress [8, 9, 10] and the scientific case has strengthened further through new knowledge on how epigenetic changes might also facilitate the induction of ARE. This has led to the development of a number of synthetic inducers of the Nrf2/ARE pathway [6]. These molecules should enter clinical trials over the next few years and some may become available for Parkinson's patients in 10 to 15 year's time. There is no guarantee that they will be more effective than existing natural molecules, but we can be confident that they will be more expensive.

An extensive base of detailed scientific research, built up over twenty years by many leading research teams supports the hypothesis that inducing the Antioxidant Response Element (ARE) via the transcription factor Nrf2 may be able to combat the causes of Parkinson's disease and other neurological disorders [6, 8, 9, 11, 12]. Indeed, the relation between Parkinson's disease, broccoli, Nrf2 and ARE was discussed by Simon Scott in his popular and very informative Parkinson Science blog, "The Science of Parkinson's" in 2017 [13].

Sourcing Nrf2 activators

Several activators of Nrf2 can be found in food. Common food sources include cruciferous vegetables, rosemary and turmeric. To be effective, the active molecules must be present and bio-available in sufficient quantity to enable a therapeutic dose to be reached. The most intensively studied activator of Nrf2 is an isothiocyanate called sulforaphane. This molecule is not directly present in food in significant quantities, but can be produced from a precursor molecule, a glucosinolate called glucoraphanin found in the seeds of cruciferous vegetables (the *Brassica* family) such as broccoli, cabbage or brussels sprouts. The vegetables themselves contain only small quantities, but the seeds and early seedlings are very rich in glucosinolates.

However, it's rather more complicated than that – which is why I made a huge beginner's mistake!

Each variety of the *Brassica* family produces a different type or a range of different glucosinolates in the seeds. It is therefore important to select the precise variety to know which glucosinolate is dominant because each different glucosinolate will be transformed into a different isothiocyanate. Even varieties sharing the same Latin name can have different glucosinolate profiles. Relying on the common names can be particularly misleading. In my early trials, I used a French brand of broccoli seeds, available from the local organic food shop to grow broccoli sprouts. It was labelled "Brocoli Bio", an Italian variety of so-called mini-broccoli or "Brocoletto".

Some weeks later, when I mentioned the origin of my seeds to a distinguished plant expert, Dr Maria Traka, Deputy Head of Food Databanks National Capability (FDNC), Quadram Institute, Norwich UK., I received the following reply: *"The online link describes the seeds as Brassica rapa cymosa and I am sorry to say that this is not broccoli (Brassica oleracea var italica). More to the point B. rapa has a totally different glucosinolate profile, dominated by gluconapin (3-butenyl glucosinolate), glucobrassicanapin (4-Pentenyl glucosinolate), and progoitrin. Unfortunately, there is a miniscule amount of glucoraphanin (the precursor of sulforaphane) if not absent altogether. Gluconapin is pungent and would account for the 'burning sensation' you describe."*

Professor Richard Mithen, Chief Scientist, High Value Nutrition National Challenge, The Liggins Institute, University of Auckland, NZ added : *"B.rapa seeds accumulate 3-butenyl glucosinolate, which will have generated 3-butenyl isothiocyanate. This chemical is very similar to sulforaphane (4-methylsulphinylbutyl isothiocyanate) but is more volatile and has a pungent odour. It is the main isothiocyanate in Dijon mustard manufactured from B.juncea. It is harder to work with than sulforaphane due to its volatility (which makes it hard to quantify) and has been less attractive for use in food products due to its organoleptic properties,* ***but is very likely to have much the same biological activity as sulforaphane."***

I received this expert information only after I had completed the first and most important phase of my experiments with the extract from the "Brocoli Bio", *B. rapa* cymosa seeds. It corrected my initial belief that I had been working with *sulforaphane*, when in fact the active substance was *3-butenyl isothiocyanate*. I would like to thank Dr Maria Traka and Prof. Richard Mithen for putting me on the right path.

Extracting isothiocyanates from *Brassica* sprouts or seeds

The relationship between the consumption of cruciferous vegetables and the beneficial effects on health is well established. It has been particularly well demonstrated to be protective against several forms of cancer and neurological disorders [14, 15, 16]. Fahey, Zhang and Talalay [17] pioneered the use of broccoli sprouts as a rich source of inducers of detoxifying enzymes as protection against

carcinogenesis. 3-day broccoli sprouts contain 10-50 times more active glucoraphanin (the precursor of sulforaphane) than do mature plants. Over the years, trials relating to various conditions from cancer to diabetes to autism have been evaluated using broccolis sprouts and later using standardized extracts of sulforaphane [18, 19].

The intrinsically healthy idea of using broccoli sprouts as a daily controlled source of isothiocyanates to explore up-regulating Nrf2 was of course a factor in my choice of the misnamed “Brocoli Bio” *B. rapa* cymosa seeds sold specifically for this purpose. This method rapidly came up against the need for regular daily preparation of sprouts and the constraints of daily life with periodic absences. It takes approximately 8 days from the moment of soaking the dry seeds through germination to harvesting 3-day broccoli shoots. For consistency, 8 daily stages of production are therefore required to provide a regular supply of the sprouts at a more or less constant growth stage. During this period of development, the glucosinolate content of the seed is almost totally transferred to the sprouts as the water content increases considerably [17]. Using seedling weight is not an ideal proxy measure for the quantity of glucosinolates in successive day-to-day batches. For these practical reasons, I therefore abandoned the culture of broccoli sprouts and reverted to the more reproducible method of using dry seeds which are an even richer source of glucosinolates than sprouts.

Isothiocyanates are formed by hydrolysis of their glucosinolate precursors through the action of the enzyme myrosinase, also present in *Brassica* plants [17]. The process is temperature-sensitive and can take several routes, one leading to the formation of the biologically-active isothiocyanate and others leading to the formation of inactive compounds [20]. The defining factor is the presence of a heat-sensitive protein called epithiospecifier protein (ESP) which modifies the product of the enzyme hydrolysis with the formation of a nitrile compound rather than the isothiocyanate [20]. Other researchers have reported even more complex pathways with even lower yields of isothiocyanate [21]. Fortunately, ESP can be inactivated by heat treatment. The optimum conditions for isothiocyanate conversion would appear to be in the range 55-65°C. At lower temperatures, the inactive nitrile compound is formed and at higher temperatures the myrosinase enzyme is also inactivated. Interestingly, myrosinase present in white mustard or Daikon radish seeds is more efficient and more specific at producing isothiocyanates than that of other *Brassica* species. They can therefore be used in addition or as a replacement for endogenous myrosinase when using other *Brassica* seeds [17].

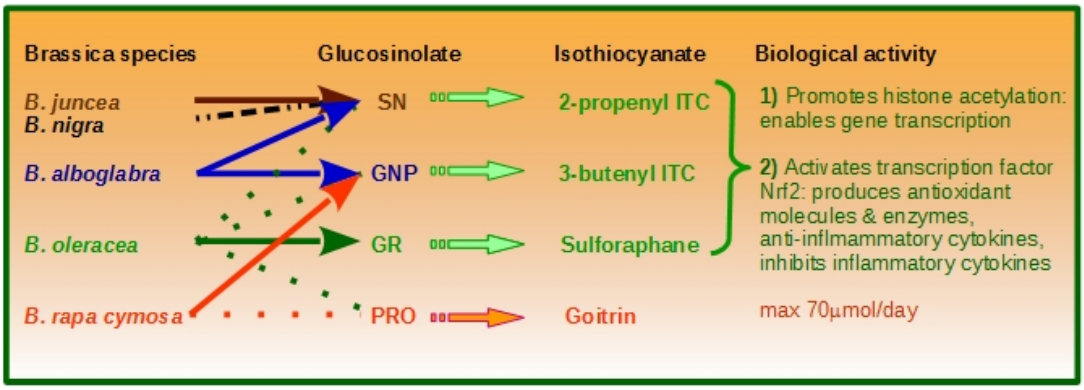
The procedure I adopted was as follows: *Brassica* seeds were first dry heat treated in vacuum sealed sachets at 55-60°C for 10 minutes to inactivate the ESP protein. 10% white mustard seeds (synapis alba) or Daikon radish seeds, was then added and the mixed seeds were ground together in a domestic coffee grinder to make a relatively coarse powder. A typical batch size was about 25g. This powder has the advantage to be perfectly stable for several days if kept in a dry container at ambient temperature. 200 ml of fresh water was heated in a small pan to 60 ± 2°C. 2-3g of seed powder added and stirred for 5 mins at 60°C before being filtered through a fine tea strainer. The filtrate produced is a cloudy yellow liquid. Depending on the variety of seeds used and the isothiocyanate profile produced, the filtrate may have a musty smell and an unpleasant taste with a transient burning sensation at the back of the throat. Since the isothiocyanates may be volatile and have limited stability, the extract has greatest potency if consumed warm immediately after being produced. There may be other and certainly better ways of extracting isothiocyanates, but this method is relatively practical and has produced the results given below. I calculated that 2-3g of seeds should produce a daily dose of up to 100 μmol of isothiocyanate, a quantity typically used in sulforaphane trials for other conditions. This will of course vary according to the *Brassica* species and variety used and the rate of conversion of the glucosinolate to the isothiocyanate. Since I had no means of measuring this, the actual isothiocyanate dose may be quite significantly different from my initial estimation.

Selecting Brassica species

Scientific research on isothiocyanates for medical use has been dominated by sulforaphane. The reasons for this are essentially due to the practical issues of its relative stability and ease of use. As a result of this extensive research, it is considered to be safe and forms the cornerstone of many research programmes.

The other isothiocyanates have not been studied in such great detail for medical use, but several others are of interest. These include 2-propenyl isothiocyanate, also known as allyl isothiocyanate or AITC and 3-butenyl isothiocyanate. All three are small molecules potentially capable of crossing the blood-brain barrier and activating both histone acetylation and the Nrf2 pathway in brain cells.

There are literally hundreds of *Brassica* varieties each with their own glucosinolate profile from which different isothiocyanates can be extracted. To review the glucosinolate profiles and related isothiocyanates of the most important *Brassica* varieties see [22, 23, 24]. The glucosinolates profiles can also vary among different cultivars and may be dependent on climate and growth conditions [25, 26]. There is not total consistency among the data, partly due to the experimental techniques used and partly due to natural variance, but the major trends are well defined. This enables the selection of a range of *Brassica* species which could be used to produce the desired isothiocyanates and to avoid the toxic ones. The principle is shown in the following diagram (data from ref. [22]). Other choices are possible, but this small group would seem to be a good starting point.



Brassica species accumulate different glucosinolate profiles which can be converted to isothiocyanates by the enzyme myrosinase. Three small isothiocyanates are likely to be particularly active in the brain.

***B. juncea*, (brown mustard) *and B. nigra*, (black mustard)** produce mainly 2-propenyl ITC or allyl isothiocyanate. This small molecule is very likely to be highly active in the brain.

***B. oleracea var italica*, (broccoli)** is rich in glucoraphanin, the precursor of sulforaphane the largest, most stable isothiocyanate of the group. Other *B. oleracea* varieties include cabbage and brussels sprouts but the glucosinolate profile can vary significantly [22]. They may include very small amounts of goitrin, a toxic substance which can affect the production of thyroid hormones when consumed at elevated levels. Given the extensive research on sulforaphane, this would be the most appropriate candidate for further research.

B. rapa cymosa*,** produces mainly 3-butenyl ITC. This isothiocyanate is volatile and is responsible for the pungent smell and taste of mustard, horseradish and wasabi. For these reasons it has not been a favoured substance for scientific research. It is however likely to be highly biologically active. There are many varieties of *B. rapa including* chinese and japanese varieties such as ***B. rapa

***japonica* (mizuma)** which have quite different glucosinolate profiles that are well worth exploring [21].

***B. oleracea alboglabra* (F1 Chinese kale variety)** is rich in both 2-propenyl ITC and 3-butenyl ITC and is free from goitrin. As such it is potentially an excellent choice for sourcing isothiocyanates. However, the seeds (sold in small quantities for specialist gardeners) are expensive. For this reason we have not tested them to date.

Overall, the complexity of the glucosinolate landscape in *Brassica* vegetables and their conversion to isothiocyanates must not be underestimated. This is a subject that cannot be exploited correctly without the help of very experienced professionals. I comment on this more extensively below.

Observations with respect to Parkinson's disease symptoms

Caution In sharing this information and these observations, I would like to ask Parkinson patients to take note of the following important points:

- Although the seeds I have used here are natural products, they have been selected and processed to optimise the production of isothiocyanates. This produces a much higher dosage of isothiocyanates than usually found in food products. Isothiocyanates should be considered as drugs and may have unknown interactions with other drugs or medical conditions.
- Unless otherwise stated the observations I report are purely personal and correspond to a response to my own type and stage of Parkinson's disease. Other people may respond differently or not at all.

***Brassica rapa cymosa* extract.**
I now know that this extract most likely contained 3-butenyl isothiocyanate rather than sulforaphane as initially intended. My aim was to reach a dose of around 100 micro-mole of isothiocyanate per day, a dose recommended in various ongoing studies for other pathologies. This dose was taken in the morning while keeping all Parkinson's medication for the first 10 days (4 x cd/l-dopa 10/100mg, 3 x Ropinirole 0,50 mg). Prior to taking this extract, my Parkinson's disease symptoms were as follows: considerable fatigue, intense leg and neck pain, dyskinesia, foot dystonia, balance problems, brain fog, vivid dreams, poor sleep, urinary problems, constipation, moderate left hand tremor.

The impact of this substance was rapid and spectacular. After 5 days of treatment, almost all my symptoms, except tremor, were significantly reduced. My energy levels were extremely high. After 10 days of treatment, I was able to reduce the dosage of Parkinson's drugs by half and felt good. After 18 days of treatment I stopped all the Parkinson's drugs with no ill effects. 3 days later also I cut down on the *Brassica* seed extract in order to see if there was a durable effect.

I was able to remain free of all PD drugs and *Brassica* seed extract for 25 days without any significant adverse effects on any of the above-mentioned Parkinson's symptoms, except tremor. Tremor has continued to get worse. After this period of feeling well for the first time in two years, the effects began to wear off, so I restarted both the Parkinson's drugs and the Brassica seed extract.

4 months later and the verdict is still positive but not as bright as during those first 25 days. On the good side, neck pain, dyskinesia, foot dystonia, balance problems, brain fog, urinary problems and constipation are no longer present at this time. Leg pain, sleep and dreams are all much improved but I feel that they are getting slowly worse. Curiously, dreams are now a significant indicator of how the following day will be. No dreams = good day to follow. Periods of fatigue are variable,

especially after meals. I no longer have quite the energy I had in the early days of the treatment. Tremor continues to worsen and is now a serious problem for me.

To put this into context, like most of us, I have been living under strict Covid-19 confinement rules for the last 2 months which of course has a serious impact on morale and my psychological well-being. Nervous stress is well known to have an adverse effect on tremor.

Discussion

As a researcher, I found these observations rather convincing since they appeared to support my initial scientific reasoning. On the other hand, I have no valid explanation for the early euphoric period where I was able to go without all PD drugs and seed extract, nor for the decline thereafter even when resuming seed extract and prescription drugs. An interesting observation is the total disconnect in changes between tremor and the other PD symptoms. Could this be telling us something about the relation between the causes of PD and those of tremor?

As a patient, I am hopeful but more reserved. For 25 days I felt almost cured (except for the tremor), but it didn't persist at that euphoric level. I have had some bad days since then during the Covid19 confinement period. I have since largely recovered, but only with the combination of levodopa and the seed extract. The initial effect was so rapid, unexpected and spectacular that I personally cannot imagine that such massive observations could be due to the placebo effect, but of course, I understand that the placebo effect can be important.

However, unless similar observations can be reproduced in significant patients under more controlled conditions, I do not claim that they represent anything other than anecdotal observations. For this reason, I will not make any interpretations or to draw hasty conclusions. I simply to refer to them as a set of personal observations.

I leave this research record, the methods used and the observations documented for other researchers and Parkinson's disease patients to use as they see fit. I accept that they are not perfect, and hope that they can be improved and confirmed, but for me, something actually seems to work.

If others are able reproduce similar observations in significant numbers, then we may have some new data to work on that may make sense to both scientists and patients. For the moment these observations raise more questions than they provide answers. I'm here to answer any questions you may care to ask. Unlike most other Parkinson research, this approach offers a particular advantage; the apparent speed of action of isothiocyanates on Parkinson's disease symptoms.

Unknowns, safety and risks

The health risks involved in following this method have not been evaluated, either for people in good health or for those with underlying health conditions. My own Parkinson's was getting quite worryingly worse so I took a calculated risk to try to slow down the progression. I am simply sharing what I did and what I observed. This is not an invitation to take unreasonable risks with your health. Please take medical advice before embarking upon any similar method. The health risks are unknown. The isothiocyanate profile of the extract from the seeds I used has not been chemically measured. This in itself would be a major research effort. Isothiocyanates are commonly used in food additives and as flavourings such as mustard, but the doses used here are very much higher. The minimum useful dose to provide a therapeutic effect needs to be explored. Interactions with other drugs at these doses are not well known.

A call for help from specialists, a “Scientific Council” for Parkinson sufferers

It would be great if I could honestly suggest to Parkinson’s sufferers *“Go out and buy some broccoli seeds, follow my method and make some home medication. After all, we know that sulforaphane is good for you.”* Of course I cannot do that. First of all I have no medical accreditation, so that would be unethical, but also after several months of intense research, during which I have acquired a very basic knowledge of the subjects and processes involved, I fully realise that this subject is much more complicated than I had initially imagined. Furthermore, I do not have the expertise or the resources to take this much further alone. The next step, even a modest one, will need the support of a team of specialists. This support could take the form of a “Scientific Council for Parkinson’s sufferers”, specialists from many disciplines that we can call on for expertise and guidance. I made a stupid beginner’s mistake in my own experiment. I want to avoid another.

In addressing these specialists, I would say this *“You can choose to play a prominent role or simply remain in the background. However your expertise and your experience will be vital to help patients make informed decisions. These are often simple decisions, in this case, such as which seeds or standardised preparations to choose and why? Or guidance about how to design a good patient-guided experiment? I believe that membership should be made up of both scientists and Parkinson patients with scientific knowledge. I, or others can play the role of secretary if necessary to filter and reformulate questions. Your individual responsibility should of course be protected.”*

A “Scientific Council for Parkinson’s disease may just be a first step. There could be several branches for different fields. We may also need to think about creating a structure or raising funds for this kind of research. It is too early to take action on that right now. We need more data and a clear roadmap. I invite both researchers and Parkinson patients send me their views on this.

My idea is to give the patient more direct access to the latest scientific knowledge to help him/her make better informed decisions on how to deal with this disease on a personal level. Can we use this isothiocyanate research subject to bring patients and specialists together? Are there ethical issues to be solved? Of course, there are many questions to answer, but I believe we could all learn a great deal from such an adventure.

With a collective effort of this kind, research of this nature would have a greater chance of making progress. I hope you will join me.

Albert Wright

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