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Apitherapy as a possible complementary treatment for Parkinson's disease

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Abstract---Parkinson's disease (PD) is becoming increasingly prevalent in Algeria. Nonetheless, only few studies were carried on this very common neurodegenerative disease in the country, especially in the wilaya of Tlemcen. The medical treatment of PD only offers symptoms relief care and is usually expensive. That is part of the reason why great interest is given to Apitherapy treatments nowadays. Alternative medicine, especially Apitherapy is included in complementary and integrative medicine, which was the goal of our study. Part of our extended study on PD aimed to investigate the effect of Apitherapy, using propolis, bee pollen, honey, and royal jelly. 60 Parkinson patinas immersed in the ON phase of the disease added an Apitherapeutic treatment with their previous treatments. We noted that with the association of the Apitherapeutic treatment and the basic treatment, the motor signs have diminished. 78.3% of the cases have passed from the ON phase to the OFF phase. In addition, we confirm that the used Apitherapeutic treatment in association with the basic treatment proves to be very effective unlike when either of them is used alone.

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Introduction

Parkinson's disease (PD) is the second most common neurodegenerative disease after Alzheimer's (ref). The incidence of this disease increases with age; estimated at 1% over 65 **(Lau and Breteler., 2006).** Parkinson's disease results from the loss of dopaminergic neurons in the substantianigra accompanied by the disruption of a whole network of neurons associated with them at the level of the thalamus, the subthalamic nucleus, the striatum, and many other cervical areas, leading to a variety of motor and non-motor clinical characteristics expressed at all stages of the disease **(Massano*and* Bhatia, 2012).**

The current treatments merely offer symptomatic alleviation and leave nondesired side effects. Plus, the enormous expense of its care burdens the public healthcare systems. Hence, recent researches have focused on the use of alternative medicine, particularly Apitherapy, as potential pharmaceuticals to slow the disease's progression **(Alvarez-Fischer *and al.*, 2014).**

Apitherapy is a form of complementary medicine that uses various bee products as therapeutic agents to ward off illnesses and slow the progression of the disease **(A. Nitecka-Buchta*and al.* 2014)**. Recently, research into using natural products to prevent or treat various diseases has become more popular, Apitherapy and bee products in particular are gaining huge popularity **(Lee J.D *and al.*, 2005; Fratellone, 2015; Bognadov, 2020; Doko *et al.*, 2020).** In many nations nowadays, Apitherapy is included in complementary and integrative medicine. Additionally, the use of bee products as nutraceuticals and nutritional supplements has expanded because of their nutrients **(Pasupuleti *andal.*, 2017; Al Naggar*and al.*, 2021).**

In Algeria, alternative medicine has always been a go-to treatment in many illnesses. Perhaps that comes from a traditional and cultural point of view, as our ancestors always used Apitherapy in prevention and treatment. Nowadays, Research on using bee products as therapeutic targets is growing **(D. Alvarez-Fischer *and al.* 2013;J. Kocot*and al.* 2018).** The beehive produces a large number of products loaded with bioactive ingredients such as propolis, bee pollen, honey, royal jelly (RJ), and bee venom **(L. Cornara,*and al.*2017).** There are many medical records of the usage of royal jelly all over the world, it has been mainly used in Asia. Recent reports indicated a high potential of this natural product to improve human health**. L. Cornara,*and al.*2017)**

Part of our extended study on PD aimed to investigate the effect of Apitherapy, using propolis, bee pollen, honey, and royal jelly. In addition to the main objective raised, and given the relatively rare or even non-existent data on this pathology in Algeria especially in the Wilaya of Tlemcen, our study will offer insights for fruitful use of bee products in future clinical trials.

Materials and Methods

Studied population:

The present study was performed between january 2022 and June 2022, this is a population-based, nested cohort study of a sample of 60 patients (32men and 28 women, aged between 61 and 90, who represented average and bad evolution (61.7% and 38.3% respectively), from our global study which represented an epidemiological study on 300 parkinsonians Recruited in the medical office of Dr. Chahrazed Belabid. All the subjects of the study reside in the wilaya of Tlemcen. There all consented freely to participation in the study.

A questionnaire on lifestyle, personal and family medical histories, current medication and socioeconomic and educational levels was completed during a face-to-face interview
All patients were under a dopamine and other treatments for more than a year and expressed either an average or a bad evolution of the motor symptoms (figure 4),

The statistical analysis of the data was carried out using the SPSS 23rd Version software and the Minitab software where we have entered the information that our questionnaire contains and we used the khi-2 tests, as well as the degree of freedom and the p-value tests (table 1/2) additionally the EXEL 2016, Also the evolution of the disease was realized by the UPDRS scale

Apitherapeutic treatment

The followed Apitherapeutictreatment was proposed by Prof. Gaouar Semir Bechir Suheil, and it was based on treating with products harvested, transformed, or secreted by the bee like honey, propolis, pollen, and royal jelly.

The apitherapeutic recipe:

The apitherapeutic used protocol is detailed as follows:
Mix 20 grams of royal jelly with 20 grams of propolis with a quarter of fish liver oil, and then cute it into 42 portions. After take a portion under the tongue 15 minutes before eating (3 times a day).
Boil a quarter of a liter of water with an addition of two table spoon of marjoram and then close it for 10 minutes, then filter it with an addition of a table spoon of pure honey(taking into account that if the patient has diabetes a tea spoon is considered sufficient) with a tea spoon of pollen and ground currant then drink it warm in the morning on an empty stomach at breakfast and at dinner time
Put drops of olive oil in the nostril (At first put only just 2 drops in each nostril and with the passage of a week put 21 drops in each nostril)
The experiments were carried our 60 patients of different sexes who were also given verses from the Holy Quran to listen to within a specific period of time.

Results

Before Apitherapy:
Before Apitherapy, the evolution of PD was independent of age groups, sex, marital status, and profession with all p-values greater than 0.05.

Table 1: Results of the study before the Apitherapeutic treatment

Parameters		Bad evolution	Average evolution	Khi-2	DDL	P value
Age	<60 years-old	6	6	1,320	3	0,725
	61-70	10	21			
	71-80	4	5			
	81-90	3	5			
Sex	Men	10	22	1,455	1	0,228
	Women	13	15			
Marital Status	Married	18	32	0,691	1	0,406
	Widower	5	5			
Profession	Employee	10	21	1,001	1	0,317
	Unemployed	13	16			

The evolution of bad and average cases that treats with the original treatment is shown in figure 1. 38.3% had a bad evolution, and 61.7% represented an average evolution.

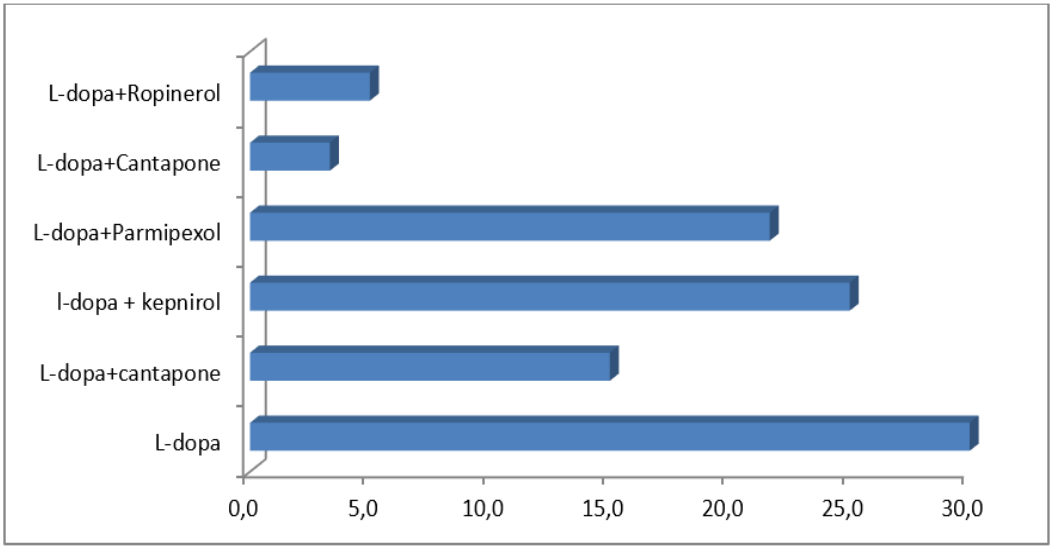

Figure 1: the basic treatment of patients before apitherapy

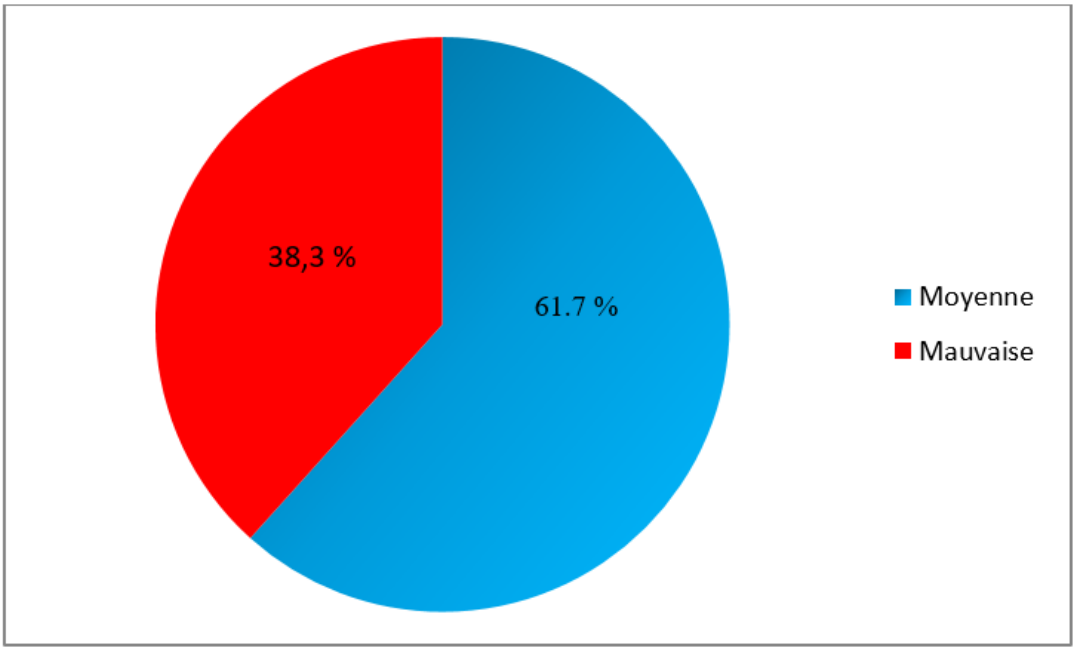

Figure 2: Distribution of Patients according to evolution with the original treatment

The evolution of the motor symptoms while using the original treatment decreased moderately for majority of the symptoms. However, for those representing a bad evolution it decreased slightly according to figure 2.

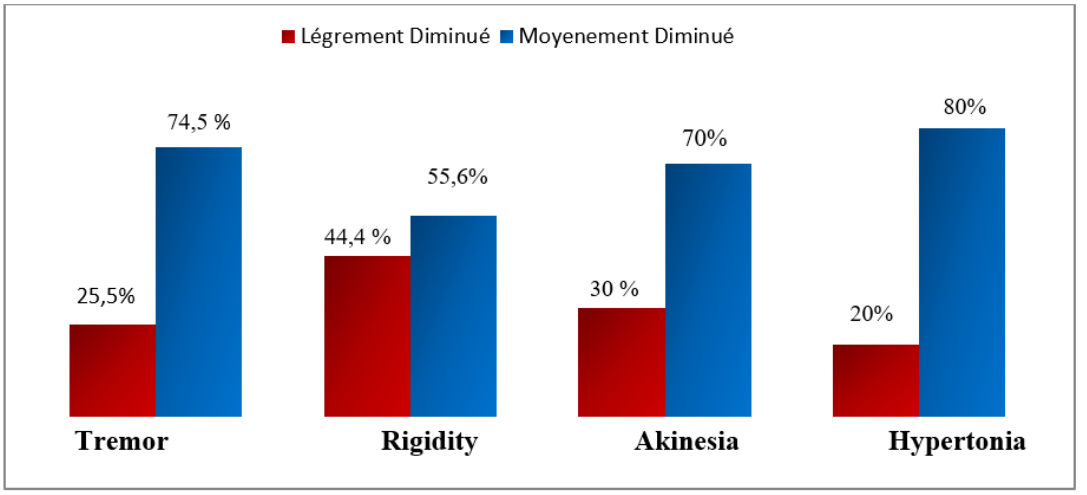

Figure 3. The evolution of the symptoms of most concern with the original treatment

Association of the treatments:
86.7% of the patients followed the recipe while 13.3% of them did not follow it correctly (figure 4).Depending on the combination with the original treatment, the

majority of our patients who agreed to stop the medical treatment gradually resumed it a short while after stopping it 31.7%. While 46.7% of them continued both treatments from the beginning and 21.7% have reduced the original treatment (figure 4).

After Apitherapy:

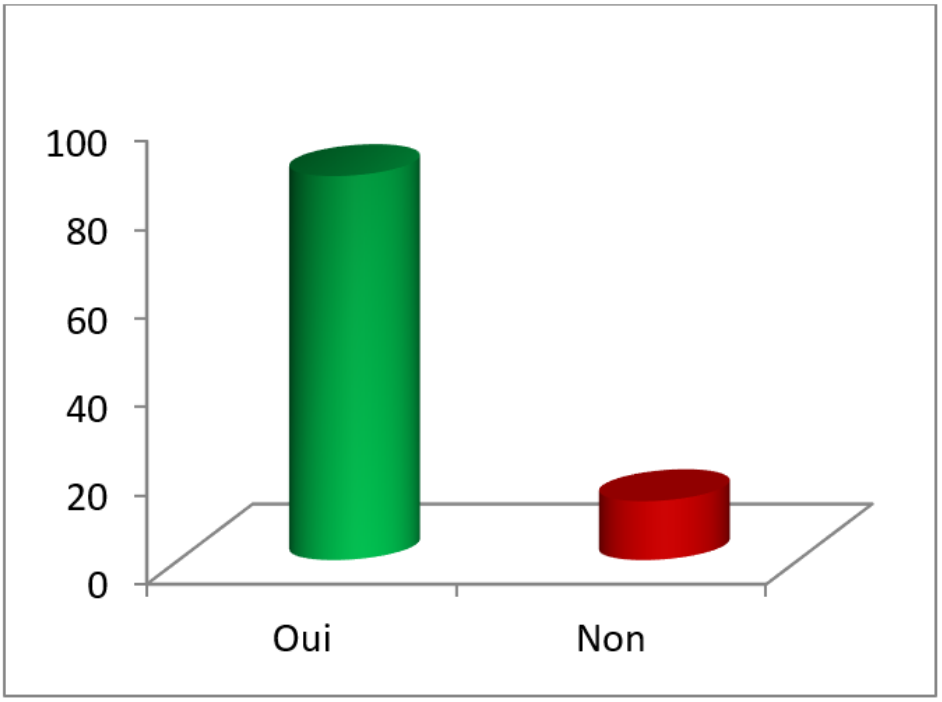

Figure 4. Distribution of patients according to compliance with the recipe

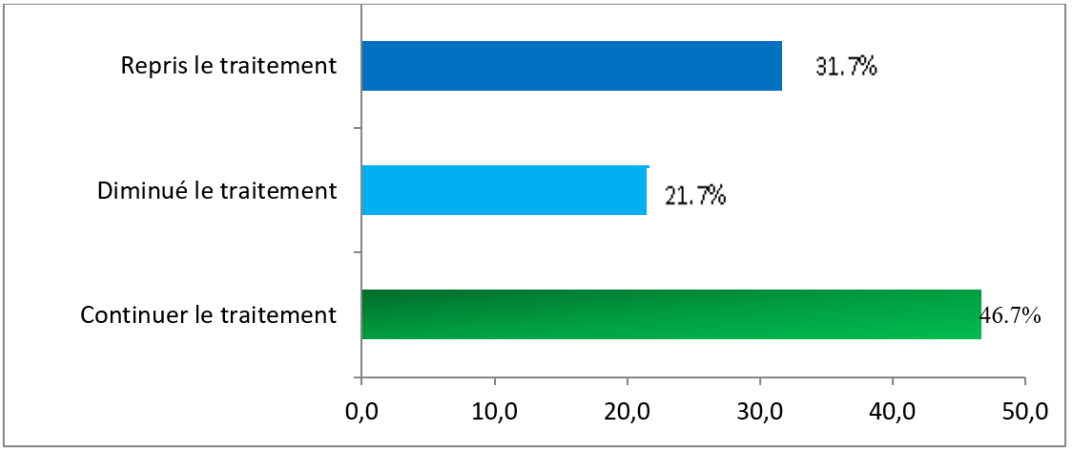

Figure 5. According to the association with the original treatment

After the Apitherapy treatment, no association between the evolution of Parkinson's disease and age groups (p=0.904), sex (p=0.815), marital status

(p=0.513), and occupation (p=0.537) was observed. However, we noticed that most patinas leveled up to a good evolution of the motor symptoms with the treatment. The evolution with the original and Apitherapeutic treatment; with the association of the Apitherapeutic treatment we note a good evolution and that in 78.3% of the cases. 10% had an average evolution and 11.7% represented a bad evolution (table 2) and (figure 5)

Table 2: Study results after Apitherapeutic treatment

Parameters		Bad	Average	Good	Khi-2	DDL	P value
Age	<60 yearsold	1	0	11	2,168	6	0,904
	61-70	3	5	23			
	71-80	1	1	7			
	81-90	2	0	6			
Sex	Men	3	3	26	0,410	2	0,815
	Women	4	3	21			
Marital Status	Married	6	4	40	1,335	2	0,513
	Widowed	1	2	7			
Profession	Employee	5	3	23	1,242	2	0,537
	Unemployed	2	3	24			

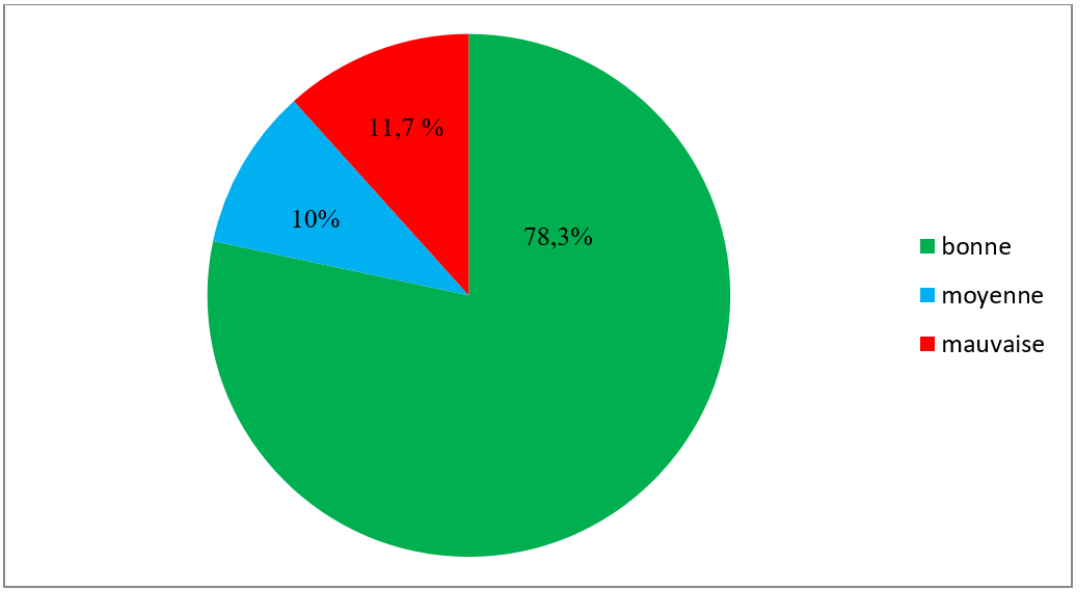

Figure 6: evolution with the original and Apitherapeutic treatment

As for the evolution of the most common symptoms with the original and Apitherapeutic treatment; the majority of symptoms have decreased after the combination of Apitherapeutic treatment. Tremor symptom has decreased to 78.7%, Rigidity decreased to 62.5%, Akinesia to 82.8%, and 100%of the hypertonie was cured.

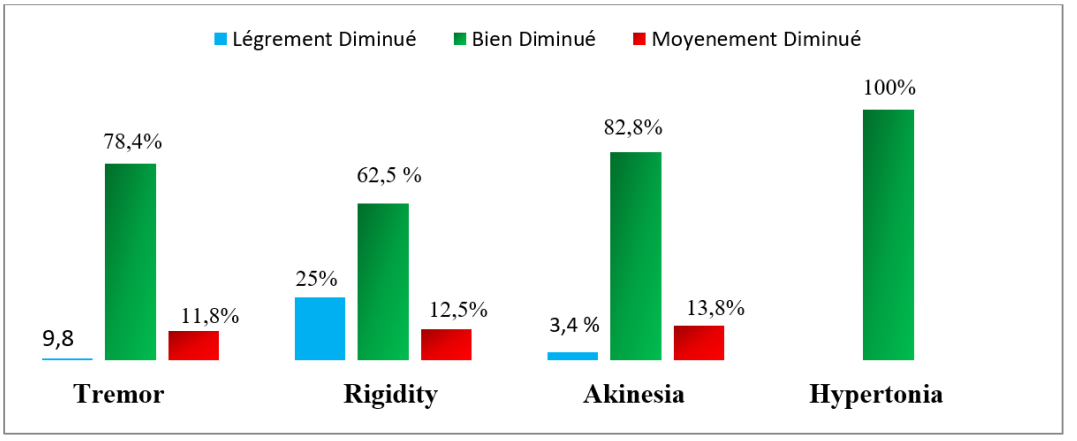

Figure 7: Evolution of the most worrying symptoms with the original and apitherapeutic treatment

The evolution of patient relief during the 6 months of Apitherapeutic treatment: We notice that the patients as the months go by begin to relieve themselves. This is following the improvement of the motor symptoms, which translates into a stabilization of 18/20 this on the majority of cases during the 6 months.

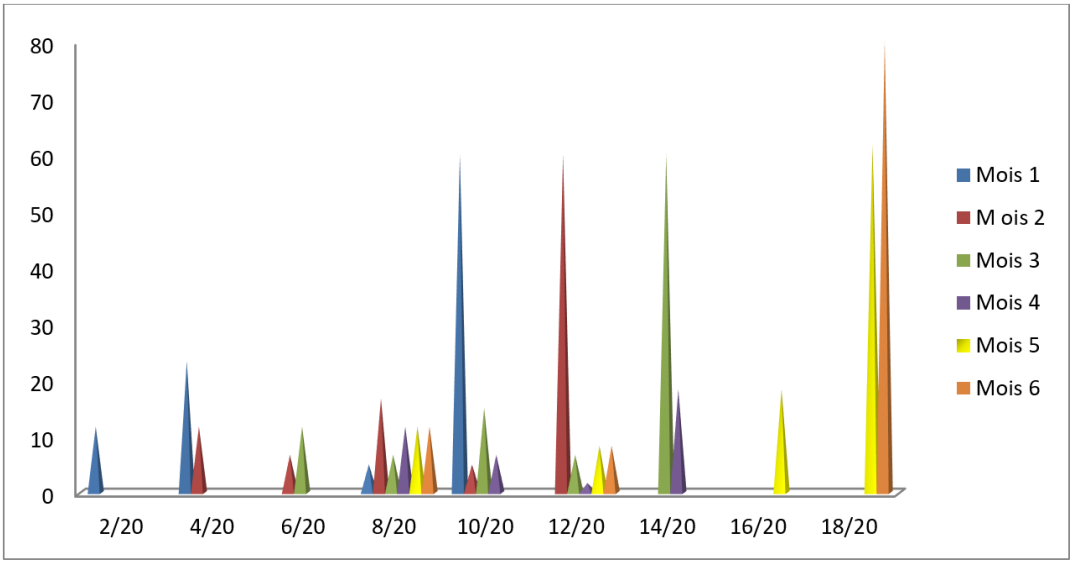

Figure 8: The level of relief of patients during the 6 months of Apitherapeutic treatment

Discussion

In our apitherapeutic study which was carried out on 60 parkinsonians immersed in the ON phase, where the patient is in a phase of cessation or blockage during which the drug and its effects fade and the motor signs reappear, unlike the phase OFF. In order to help these patients get out of their blockage and find a stabilized state, apitherapy was the best way we could find. For this we allowed

ourselves to explore the epidemiological aspects of the evolution of their condition before and after the apitherapeutic treatment.

Our results indicate that before apitherapy, the evolution of PD was independent of age group, sex, marital status and occupation with p-value values greater than 0.05. The same result was obtained after apitherapy, with no association between the evolution of PD and age groups (p=0.904), sex (p=0.815), marital status (p=0.513), and the profession (p=0.537) is observed. Our apitherapeutic study is the first of its kind in Algeria. 53.4% of our patients who had agreed to stop treatment to follow apitherapy only, found themselves in a state of total blockage; 31.7% of them resumed their treatment and 21.7% reduced it, while the recipe was respected by the majority of them.

We note that with the association of the apitherapeutic treatment and the basic treatment the motor signs have diminished. In 78.3% of the cases have passed from the ON phase to the OFF phase, which explains the good improvement of the signs motors, and Confirm that the apitherapeutic treatment: propolis, royal jelly, pollen, etc. in association with the basic treatment proves to be very effective unlike that alone.

Very few preclinical studies have evaluated the effect of propolis flavonoids, royal jelly and these lipids on PD **(M. Taherianfard *and al* 2017).** The protective effects of these compounds are likely attributed to their ability to reduce the production of free radicals (H. Wang, et al 2016), pro-inflammatory cytokines and mitochondrial proteins involved in cell death as well as their downstream effectors such than caspase-3 **(Y. Wang, J. *and al* 2014).**

Immunochemistry and cell viability analyzes revealed higher survival of dopaminergic neurons treated with these compounds both in vivo (CV Fontanilla et al 2011;ATR Goes, et al 2018; SA Zaitone, et al 2019; et in vitro Y. Inoue et al 2018). These results, as well as ours, indicate that bee products such as propolis and royal jelly may be a potentially safe adjunctive treatment for PD. From a theoretical point of view, propolis and jelly and honey may be beneficial not only for the main motor symptoms of PD, but also for other non-motor symptoms such as cardiac, autonomic, gastrointestinal symptoms, depressive and cognitive **(P. Perez-Pardo *and al* 2017).**

Thus, we suggest that propolis and royal jelly may positively affect the gut-brain axis in Parkinsonian patients by modulating the composition of the microbiota. Future studies exploring the effect of bee products on the microbiota in PD and its association with molecular and cellular adversities associated with PD will provide relevant information. It might be useful to compare the effect of the combination of propolis and RJ with other conventional treatments such as dietary modifications and exercise since these interventions express their effects, in part, through the modulation of microflora intestinal **(SF Clarke, *and al* 2014).**

A study done by **Ali Ali Gobaili Saged and al** has empirically proved that the sound of the Holy Quran is an effective treatment for those who suffer from spiritual and psychological issues, The results of the effectiveness factor came

after ability and willingness and gave a result of 92.6% for those who support the contention that the Quran has a significant healing influence. Also, some of the patients who regularly attended Quranic therapy sessions have been successfully cured, 81.8% of the sample believe that Quranic therapy sessions support their health needs***.(Ali Ali Gobaili Saged and al 2020)***

Another study done by Abdel Aziz et al. investigated the effects of honey on HepG2 cell lines. The report showed that honey exerted cytotoxic, antimetastatic, and antiangiogenic effects on HepG2 cells based on different concentrations **(A. Abdel Aziz, and al 2009)**

Honey has also a beneficial effect on pediatric dermatitis caused by excessive use of napkins and diapers, eczema, and psoriasis. The effect of honey mixed with bees wax and olive oil was investigated on patients with psoriasis or atopic dermatitis condition. A clinical trial showed that a mixture containing honey was extremely well tolerated and caused significant improvements. Honey consists of various nitric oxide metabolites, which reduce the incidence of skin infection in psoriasis ***(N. S. and al 2003)***

Alzheimer's disease are the most common among the elderly. Royal jelly seems to stimulate the mental functions through its neuroprotective effect. Daily intake of royal jelly was reported to consolidate the memory abilities and learning skills in honeybees and rats(**Zamani, Z. and al 2012)**

Royal jelly intake is efficient for the alleviation of menopause-related neurological disorders, but the mechanisms of action remain to be better described. However, the decrease of cholesterol and beta-amyloid levels, the increase of estrogen levels, and the improvement of blood-brain barrier seem to be the most mentioned mechanisms by which royal jelly exerts its neuroprotective role **(Hattori, N.and al 2006)**

Furthermore, this natural product stimulates neurite outgrowth, induces the regeneration of hippocampal granule cells, and protects the central nervous system against oxidative injuries (**Cihan,Y. and al 2014)**

Conclusion and perspectives

PD is characterized by a set of motor signs, of which tremors and akinetic disorders are the most common in our population, and non-motor signs most often represented by neuropsychiatric disorders. To date, there is no cure for Parkinson's, but drug strategies have been developed and dopatherapy is the most effective treatment for the majority of patients. our apitherapeutic study was carried out on 60 parkinsonians immersed in the ON phase, In order to help these patients to get out of their blockage and find a stabilized state, apitherapy was the best way we could find, We find that 'with the combination of the apitherapeutic treatment and the basic treatment, the motor signs were much reduced. In 78.3% of the cases, they went from the ON phase to the OFF phase. This explains the good improvement of the motor signs, Confirm that the apitherapeutic treatment in association with the basic treatment proves to be very effective. Let's hope that the Apitherapeutic treatment becomes more and more

popular in Algeria following its great breathtaking efficiency and for the main purpose of contributing to the development of the state with one hundred percent organic loco products.

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