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QUALIFICATION WORK

on the topic: **«DEVELOPMENT OF APPROACHES TO IMPROVING PHARMACEUTICAL CARE OF PARKINSON'S DISEASE PATIENTS»**

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ANNOTATION

In the qualification work, the issues of clinical and pharmaceutical analysis of antiparkinson medications, in particular, the fixed combination of immediate-release levodopa and carbidopa; the development of approaches to improving pharmaceutical care of Parkinson's disease treatment have been considered; the results of the survey of pharmacists and pharmacy visitors on their awareness of the aspects of levodopa/carbidopa clinical use, and recommendations for pharmacists and patients with Parkinson's disease have been developed accented on the effectiveness and safety criteria of their use in accordance with the concept of responsible self-treatment.

Key words: Parkinson's disease*,* levodopa, carbidopa*,* effectiveness criteria, safety criteria*,* pharmaceutical care

АНОТАЦІЯ

У кваліфікаційній роботі розглядаються питання клініко-фармацевтичного аналізу протипаркінсонічних препаратів, зокрема фіксованої комбінації леводопи та карбідопи швидкого вивільнення; розглянуто розвиток підходів до вдосконалення фармацевтичної допомоги при лікуванні хвороби Паркінсона; результати опитування провізорів та відвідувачів аптек щодо їх обізнаності щодо аспектів клінічного застосування леводопи/карбідопи та розроблено рекомендації для провізорів та пацієнтів із хворобою Паркінсона з акцентом на критерії ефективності та безпеки їх застосування відповідно до концепції відповідального самолікування.

Ключові слова: хвороба Паркінсона, леводопа, карбідопа, критерії ефективності, критерії безпеки, фармацевтична опіка

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ABBREVIATION LIST

AADC	–	Aromatic L-amino acid decarboxylase
AADC OR AAAD	–	Aromatic L-amino acid decarboxylase
AES	–	Adverse events
AP-CD-LD	–	Accordion Pill™ carbidopa/levodopa
CADD	–	Computerized ambulatory delivery device
CD	–	Carbidopa
CT	–	Clinical trials
COMT	–	Ccatechol-O-methyl transferase
DDC	–	Dopa decarboxylase
DPG	–	German Parkinson’s Association
GBA	–	Glucocerebrosidase
IR	–	Immediate-release
LCIG	–	Levodopa-carbidopa intestinal gel
LD	–	Levodopa
LNAA	–	Large neutral amino acid
LRRK2	–	Leucine-rich repeat kinase 2
MAO B	–	Monoamine oxidase type B
MRI	–	Magnetic resonance imaging
PD	–	Parkinson's disease
PEG-J	–	Percutaneous endoscopic gastrojejunostomy
PINK1	–	Pten-induced putative kinase 1
PK	–	Pharmacokinetics
SNCA	–	Alpha-synuclein
SSDI	–	Social Security disability insurance
SSI	–	Supplemental security income
WHO	–	World Health Organization

INTRODUCTION

Relevance of the topic. Parkinson's disease (PD) is a major neurodegenerative disease, a neuropathological disorder characterized by the degeneration of homogeneous populations of neurons (especially dopaminergic neurons) involving multiple neurotransmitter systems and multiple parts of the nervous system [1-5]. The process of denervation begins in the olfactory nucleus and the inferior nucleus of the brain stem and spreads to higher structures. The degeneration of pigmented neurons in the dense part of the substantia nigra explains many features of motor signals. The presence of residual pigmented nucleus cells and eosinophilic cytoplasmic inclusions (Lewy bodies) elsewhere in the brain is important for neuropathological diagnosis. However, Lewy bodies are not unique to PD. Lewy bodies are also seen in Alzheimer's disease and aging [1-8].

According to statistics from the World Health Organization (WHO), the incidence of PD is estimated at 4.5–16/100,000 people/year. PD is rare in people under the age of 50. Incidence rates increase with age from 5/100,000 in the 45–49 age group to 90/100,000 in the over 75 age group. Prevalence estimates range from 18 to 328/100,000. The overall prevalence of PD in patients over 65 years of age is 1.6%. Prevalence increases with age: from 0.6% in the 65–69 age group to 3.5% in the 85–89 age group [9].

The clinical diagnosis of PD requires the presence of bradykinesia and at least one of the following symptoms: tremor at rest and muscle rigidity (the main symptoms), as well as a postural reflex disorder, the so-called postural instability, which joins later. Errors in diagnosis, especially in the early stage of PD, occur frequently. However, approximately 75% of the time a diagnosis of CP is made if 2 of the 3 core symptoms are present and other neurological signs/symptoms are absent [2, 4-8, 10].

Other signs and symptoms that may be present or develop during disease progression include autonomic disturbances (sialorrhea, seborrhea, constipation, voiding disorders, sexual dysfunction, orthostatic hypotension, hyperhidrosis), sleep

disturbances, and olfaction or temperature sensation [2, 5, 11-14]. Symptoms of depression and cognitive dysfunction develop in patients with PD in almost 45% and 35%, respectively. There are no clear clinical signs that would distinguish a depressive symptom in PD from depression. As for cognitive dysfunction, the clinical and neuropathological signs are largely similar to other cognitive disorders [4, 5, 12, 14-19].

PD progresses slowly. Severe disability or death is expected in 25% of patients within 5 years of onset, 65% within 10 years, and 80% within 15 years [1, 5, 9]. When a patient has Parkinson's, you can do many things to feel in control of daily life. Everyone’s Parkinson’s is unique.

There are over 40 symptoms of Parkinson’s [2-4, 6, 17, 20]. From a tremor or stiffness to problems with sleep and mental health. Everyone’s experience is different. Common symptoms of Parkinson’s include tremors, rigidity (stiffness), slowness of movement, mild memory and thinking problems, sleep problems, pain, and mental health problems, including anxiety and depression. But not everyone gets these symptoms. People will have different experiences of how their condition changes or progresses. How Parkinson’s affects someone can change from day to day, and even from hour to hour. Motor symptoms affect your movement and balance. They include tremors, stiffness, and slowness of movement [21, 22, 20]. Non-motor symptoms affect you in other ways that may not be easily seen by other people. They include pain, sleep problems, and mental health issues [2, 6, 20]

In addition, treatment should stop further neurodegeneration and slow the progression of the disease. However, the mechanism responsible for dopaminergic cell loss in PD remains unknown. Currently, no drug treatment can significantly delay the progression of the disease.

4 ways to manage your Parkinson's symptoms [2, 4.]

I. Take medication.

There are many different drugs that can help manage the symptoms of Parkinson's:

- ✓ Levodopa (co-beneldopa and co-careldopa);

- ✓ Dopamine agonists (pramipexole, ropinirole);
- ✓ MAO-B inhibitors (rasagiline, selegiline, safinamide);
- ✓ COMT inhibitors (entacapone, opicapone);
- ✓ Amantadine;
- ✓ Anticholinergics (procyclidine, trihexyphenidyl);
- ✓ Apomorphine;
- ✓ Rotigotine skin patch (Neupro).

II. Stay active.

Being active with Parkinson's can help improve mental and physical wellbeing as well as your balance, strength and coordination (2.5 hours/week).

III. Monitoring Parkinson's symptoms.

Many people with Parkinson’s find that keeping a diary is a helpful way of monitoring their condition.

IV. Explore different therapies

✓ Occupational therapy (an occupational therapist can help do everyday tasks if they become difficult, such as moving around your home).

✓ Physiotherapy (a physiotherapist can help with posture and movement problems).

✓ Speech and language therapy (a speech and language therapist can help you with swallowing problems and any issues with your speech and writing).

✓ Complementary therapies (acupuncture, Alexander technique, aromatherapy, art therapy, Ayurveda, bowen technique, chiropractic, conductive education, Feldenkrais help, herbal medicine, kinesiology, massage therapy, meditation and relaxation techniques, music therapy, and osteopathy).

The term «late-stage Parkinson's disease» usually refers to the period when symptoms are more complex and have a greater impact on daily life. It can be helpful to plan ahead and understand what to expect in late-stage Parkinson's disease. This may be a time when Parkinson's drugs are less effective in treating symptoms or their side effects outweigh the benefits. Some people also experience changes in how their mind works. This can be a side effect of some Parkinson's drugs and can

include memory problems, hallucinations, anxiety and depression [2, 4].

Stages of Parkinson's disease

✓ Early or diagnostic stage. The time when someone first experiences symptoms, receives a diagnosis, and then comes to terms with it.

✓ Stage of maintenance. When symptoms are controlled, possibly with medication.

✓ Advanced stage. Often called the "complex phase".

✓ Palliative stage. Providing relief from the symptoms, stress and pain of the condition.

Everyone with Parkinson's disease is different, and symptoms develop at different rates. It has nothing to do with your age or how long your Parkinson's has lasted. Pharmacological treatment of patients with PD is challenging because the choice of drugs is limited, and the combination of levodopa (LD) and carbidopa (CD) is the gold standard treatment for symptom relief and quality of life [2- 4,].

Therefore, the improvement of approaches to pharmaceutical care for patients with Parkinson's disease for all participants in the treatment process, based on knowledge of the clinical pharmacology of Parkinson's drugs drugs, is of particular relevance.

The aim of the study. Therefore, the purpose of the study is to develop approaches to improve pharmaceutical care for Parkinson disease patients.

The objectives of the study. To achieve the study goals it was necessary to solve the following tasks:

1) consider the epidemiology and medico-social significance of Parkinson's disease;

2) analyze international and domestic recommendations for modern approaches to Parkinson's disease treatment;

3) create a questionnaire to conduct a survey for pharmacists about their awareness of intestinal gel containing levodopa and carbidopa use for Parkinson's disease treatment;

4) create a questionnaire to conduct a survey for pharmacy about their

awareness of the rational use of levodopa-carbidopa oral drugs for Parkinson's disease treatment;

5) develop practical recommendations for pharmacists and pharmacy visitors / patients / caregivers on the specifics of pharmaceutical care when using levodopa and carbidopa in the treatment of Parkinson's disease.

The study object. The role and place of s levodopa-carbidopa in the treatment of Parkinson's disease.

The study subject. Pharmaceutical care of Parkinson's disease patient.

The research methods. To achieve this goal, the following research methods were used:

- sociological methods of survey and questionnaire;
- methods of theoretical research;
- mathematical and statistical research methods.

Publications:

Prospects for new dosage forms of complex drugs containing levodopa and carbidopa / Zhulai T., Oklei D., Andrieieva O., Abou Warda M. // Клінічна фармація в Україні та світі : матеріали Всеукраїнської науково-практичної Internet-конференції з міжнародною участю, присвяченої 30-річчю заснування кафедри клінічної фармакології та клінічної фармації НФаУ (16-17 березня 2023 р., м. Харків). – Харків: НФаУ, 2023. – С. 135-137.

Structure and volume. The qualification work contains a summary in Ukrainian and English, an introduction, 3 chapters (literature review, materials and methods, 1 chapter of own research, discussion of the results, and practical recommendations), conclusions, and a list of used literature sources (40 references). The volume of the main text of the work is 51 pages. The dissertation is illustrated with 13 figures.

CHAPTER 1
PARKINSON'S DISEASE: A CURRENT STATE OF THE PROBLEM
(literature review)

1.1. Epidemiology and medico-social significance of PD

Parkinson's disease affects the neurological system and the areas of the body that are under the control of the nerves. It is a chronic and progressive movement disorder. It is brought on by the death of nerve cells that make the chemical dopamine in the substantia nigral, a region of the brain (Fig. 1.1). Dopamine is essential for controlling how the body moves. The primary signs and symptoms of Parkinson's disease, including tremor, stiffness, slowness of movement, and problems with balance and coordination, are brought on by a decrease in dopamine [2, 4, 6].

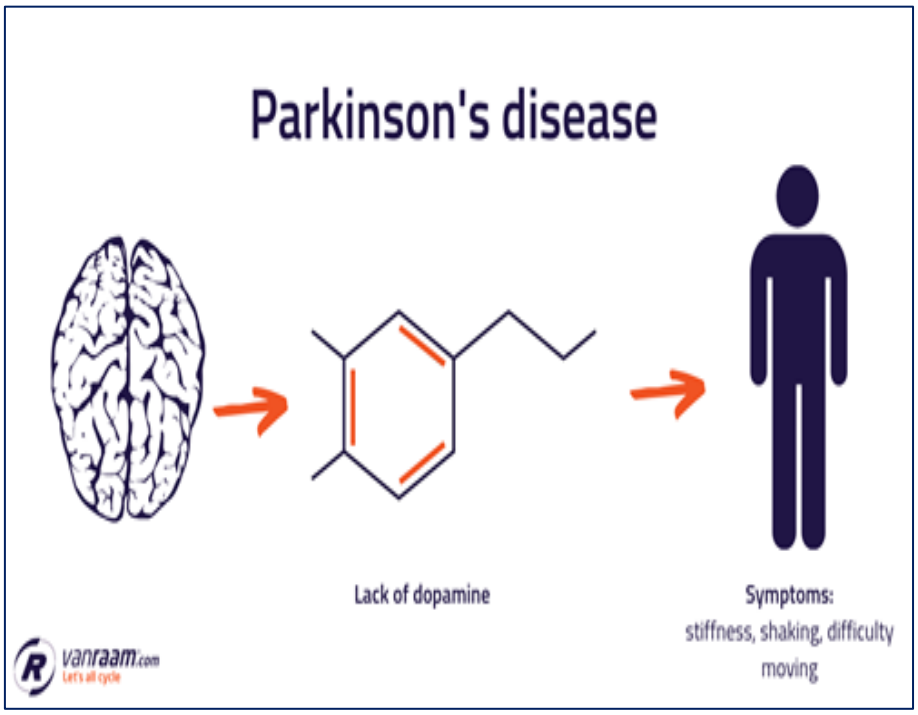

Fig. 1.1. The pathogenesis of Parkinson's disease

Symptoms of Parkinson's disease can differ from person to person. Early symptoms could be insignificant and go unnoticed. Even after symptoms start to impact both sides of the body, they frequently start on one side of the body and

usually get worse there.

Parkinson's disease has four primary symptoms (Fig. 1.2) [2, 4, 17, 23]:

- ✓ hand, arm, leg, jaw, or head trembling;
- ✓ muscular stiffness caused by prolonged muscle contraction;
- ✓ movement sluggishness (bradykinesia);
- ✓ impaired coordination and balance, which can sometimes cause falls.

Parkinson's disease can also generate non-motor symptoms such, in addition to these motor symptoms, like as [2, 4, 18, 21, 22]:

- ✓ sensory dysfunction, including loss of the sense of smell and visual disturbances;
- ✓ mood disorders, including anxiety, apathy and depression;
- ✓ constipation and gastrointestinal issues;
- ✓ fatigue, pain and cramping;
- ✓ speech difficulty, urinary incontinence, and sleep problems;
- ✓ swallowing difficulty and sexual dysfunction.

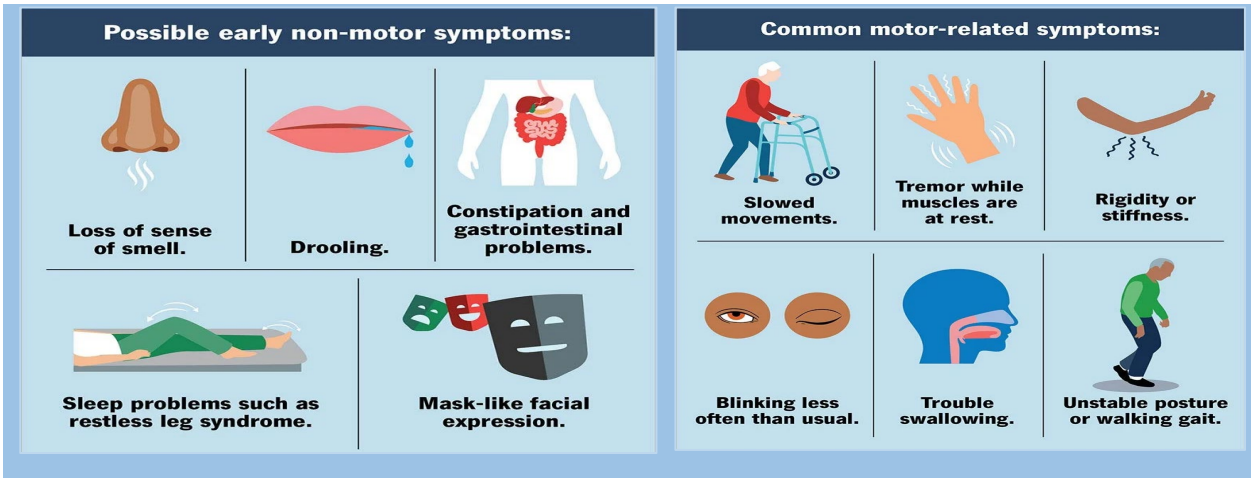

Fig. 1.2. Parkinson's disease symptoms

What are the forms of Parkinson’s disease (Fig. 1.3) [2, 4, 17, 23]?

There are different forms of Parkinson’s disease that can be classified based on the age of onset, the cause or the symptoms.

- ✓ Based on age of onset [2, 4, 17, 23]
  - Idiopathic Parkinson’s disease

This is the most common form of Parkinson's disease that usually onsets between the ages of 55 to 65 and rarely occurs before the age of 50.

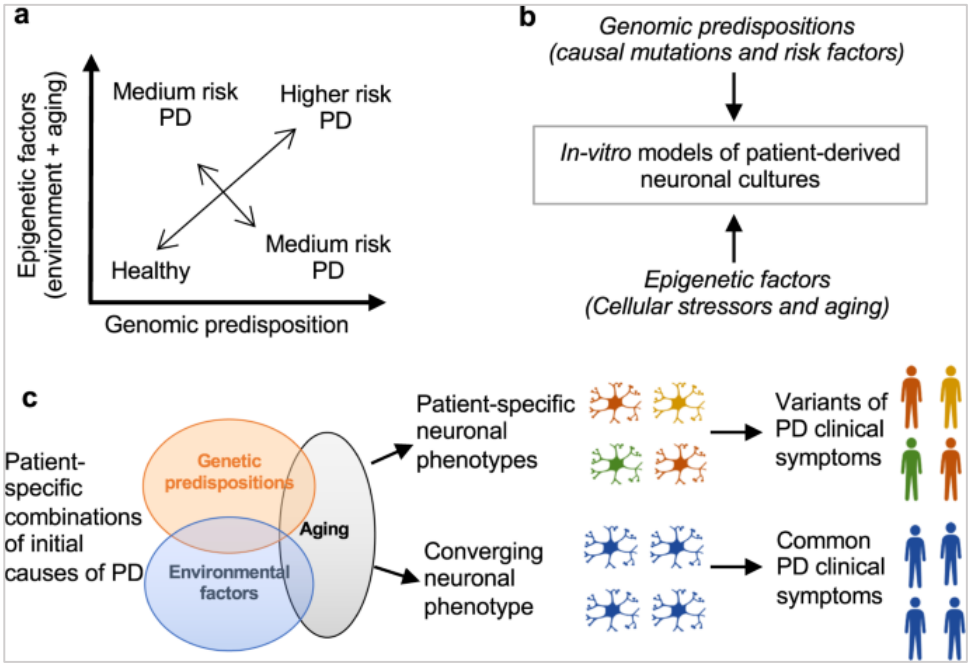

Fig. 1.3. Forms of Parkinson's disease

- Juvenile Parkinson's disease

This is a rare form of Parkinson's disease that onsets before the age of 21. It is more likely to be associated with genetic causes than late-onset Parkinson's.

- Young-onset Parkinson's disease

This refers to Parkinson's disease that presents before the age of 40. It is also more likely to be linked to genetic factors than late-onset Parkinson's.

✓ Based on cause [2, 4, 17, 23]

- Genetic Parkinson's disease

This refers to Parkinson's disease that is caused by specific genetic variants or mutations that affect the function or survival of dopamine-producing neurons. Some examples of genes that have been associated with Parkinson's disease are SNCA (alpha-synuclein), LRRK2 (leucine-rich repeat kinase 2), PARK2 (parkin), PINK1 (PTEN-induced putative kinase 1) and GBA (glucocerebrosidase).

- Environmental Parkinson's disease

This refers to Parkinson's disease that is caused by exposure to environmental

factors or toxins that damage dopamine-producing neurons. Some examples of environmental factors that have been linked to Parkinson's disease are pesticides, herbicides, solvents (such as trichloroethylene), heavy metals (such as manganese) and head trauma.

- Drug-induced parkinsonism

This refers to parkinsonism that is caused by certain drugs that interfere with dopamine transmission in the body. Some examples of drugs that can cause drug-induced parkinsonism are antipsychotics (such as haloperidol), antidepressants (such as fluoxetine), calcium channel antagonists (such as verapamil), gastrointestinal prokinetics (such as metoclopramide) and antiepileptic drugs (such as valproate)6. Drug-induced parkinsonism is usually reversible after stopping or reducing the dose of the drug.

✓ Based on symptoms [2, 4, 17, 23]

- Tremor-dominant Parkinson's disease

This refers to a form of Parkinson's disease where tremor is the most prominent symptom and other motor symptoms are less severe or absent. Tremor-dominant Parkinson's disease tends to have a slower progression and a better prognosis than other forms [18, 21-24].

Parkinson's disease (PD) is a degenerative condition of the brain that affects movement and other functions. According to the World Health Organization (WHO), over 8.5 million people worldwide are living with PD [3, 9]. The prevalence of PD varies by region, but it is estimated that nearly one million people in the US. have PD. The incidence of PD increases with age, but about four percent of people with PD are diagnosed before age 50 [9, 24].

There are different government programs that may provide benefits or assistance for people with PD, depending on their eligibility and needs [3, 4, 6]. Some of these programs are:

✓ Social Security Disability Insurance (SSDI) [3, 4, 6]

This program pays benefits to people who have worked and paid Social

Security taxes, but are unable to work due to a disability. People with PD may qualify for SSDI if they meet certain criteria and have sufficient work credits.

✓ Supplemental Security Income (SSI) [3, 4, 6]

This program pays benefits to people who have low income and resources, and are aged, blind, or disabled. People with PD may qualify for SSI if they have limited income and assets, and meet the disability criteria.

✓ Medicare [3, 4, 6]

This is a federal health insurance program for people who are 65 or older, disabled, or have certain conditions such as end-stage renal disease or amyotrophic lateral sclerosis. People with PD may be eligible for Medicare if they receive SSDI for at least 24 months, or if they meet other criteria.

✓ Medicaid [3, 4, 6]

This is a joint federal and state program that helps pay for medical costs for people with low income and resources. People with PD may be eligible for Medicaid if they meet the income and asset limits, and other requirements of their state.

This is a joint federal and state program that helps pay for medical costs for people with low income and resources. People with PD may be eligible for Medicaid if they meet the income and asset limits, and other requirements of their state.

Medication adherence is the extent to which a person takes their prescribed medications as instructed by their health care provider. Medication adherence is important for people with PD because it can improve their symptoms, functioning, and quality of life. However, medication adherence can be challenging for people with PD because they may have complex regimens, cognitive impairment, depression, or other barriers. Studies have shown that medication adherence in PD varies widely, ranging from 10% to 87% depending on the method of measurement [9, 14, 17, 25, 26].

Some factors that may improve medication adherence in PD are [3, 4, 26]:

- simplifying the medication regimen;

- using reminders or alarms;
- using pill boxes or organizers;
- educating patients and caregivers about the benefits and side effects of medications;
- addressing any concerns or beliefs that may affect medication taking;
- communicating regularly with the health care team;
- seeking support from peers or groups.

Parkinson's disease (PD), which affects movement, is a degenerative neurological condition, according to the WHO [9]. It is brought on by the death of brain nerve cells that create the neurotransmitter dopamine, which aids in controlling movement.

Around the world, PD is becoming more common. The WHO predicted that 8.5 million people worldwide were living with PD in 2019. By 2040, 12.9 million people are anticipated to be living in this country [9].

The prevalence of PD differs from nation to nation. One million Americans are thought to have PD in the country. An estimated 2.5 million people live with the condition in Europe. The prevalence in Egypt is thought to be 100,000 [9].

As you become older, your risk of acquiring PD rises. Although it can start at any age, the usual beginning age is 60. Men are somewhat more likely than women to get PD.

There is no known treatment for Parkinson's disease, however there are ways to manage the symptoms. The most popular therapies involve taking drugs that help the brain produce more dopamine. Surgery, physical therapy, and speech therapy are further therapies.

Numerous government initiatives offer assistance to those who have PD. People with PD who are unable to work in the United States can receive disability benefits from the Social Security Administration [4, 9]. For those with Parkinson's disease, Medicare and Medicaid offer health insurance. Additionally, there are several private organisations that organisations as the Parkinson's Foundation and

the Michael J. Fox Foundation, offer assistance to people with PD.

Here are several instances of government initiatives supporting people with Parkinson's disease in the US, Europe, and Egypt:

- The Social Security Disability Insurance (SSDI) programme;
- Health Insurance Parkinson's Foundation;
- Jackson Fox Foundation;
- The EPDA is a Parkinson's disease organisation in Europe;
- UK Parkinson's;
- German Parkinson's Association (DPG);
- Parkinson's Society of Egypt;
- Ministry of Population and Health.

1.2. Modern approaches to PD treatment

Comparison of the European and Egyptian guides on Parkinson's disease.

Parkinson's Europe [3, 4]

A non-profit organisation called Parkinson's Europe offers assistance and support to those who have Parkinson's disease and their family.

The website of the organisation offers a lot of knowledge on Parkinson's disease, including information on symptoms, diagnosis, treatment, and living with the disorder.

Additionally, Parkinson's Europe provides a variety of support services, including a helpline, online discussion boards, and a listing of nearby support groups.

UK Parkinson's [3, 4]

Parkinson's UK is a nonprofit organisation that offers information, assistance, and financial support for Parkinson's disease research.

The website of the organisation offers a lot of knowledge on Parkinson's disease, including information on symptoms, diagnosis, treatment, and living with

the disorder.

A helpline, online discussion boards, and a database of regional support groups are just a few of the additional support services provided by Parkinson's UK.

Egyptian Guide [3, 4]

Parkinson's Society of Egypt

The Egyptian Parkinson's Society is a nonprofit group that offers Parkinson's patients and their families support and information.

The website of the organisation offers a lot of knowledge on Parkinson's disease, including information on symptoms, diagnosis, treatment, and living with the disorder.

A helpline, online discussion boards, and a database of regional support groups are just a few of the additional support services provided by the Egyptian Parkinson's Society.

Comparison

The Parkinson's disease guidelines from Europe and Egypt include comparable details on the condition's signs and symptoms, diagnosis, therapies, and quality of life. There are minor variations between the guidelines, though.

The guides from Europe are more thorough than the one from Egypt. They offer a greater range of services and more details on the most recent research on Parkinson's disease.

The needs of Egyptians with Parkinson's disease are given more attention in the Egyptian guide. It offers details about neighbourhood resources and services that aren't offered in other nations.

1.3. Clinical and pharmacological characteristics of Parkinson's drugs

There are many different drugs that can help manage the symptoms of Parkinson's [2-4, 17, 18, 23, 27-30].

Dopamine is a chemical messenger made in the brain. The symptoms of Parkinson’s appear when dopamine levels become too low. This is because cells in

your brain that produce dopamine have stopped working.

The drugs take for Parkinson's will do one or more of the following:

✓ increase the amount of dopamine in the brain;

✓ act as a dopamine substitute, stimulating the parts of the brain where dopamine works;

✓ block the action of other factors (enzymes) that break down dopamine.

The main groups of Parkinson's drugs are presented in Fig. 1.4.

Parkinson's drugs

Levodopa (co-beneldopa and co-careldopa)

Dopamine agonists (pramipexole, ropinirole)

MAO-B inhibitors (rasagiline, selegiline, safinamide)

COMT inhibitors (entacapone, opicapone)

Amantadine

Anticholinergics (procyclidine, trihexyphenidyl)

Apomorphine

Rotigotine skin patch (Neupro)

Fig. 1.4. The main groups of Parkinson's drugs

Drugs for Parkinson's can be divided into three categories [2-4, 17, 18].

- The class or type of drug – levodopa.
- The generic (unbranded) name, such as co-beneldopa (a combination of levodopa and benserazide).
- The brand name – Madopar is the name that the pharmaceutical company, Roche, uses to sell co-beneldopa.

Modified release, controlled release and prolonged release medication [31]

May see that medication is written as modified release. It can also be written as controlled release (CR) or prolonged release (PR). All of these labels mean the same thing but drug companies can choose which one to use with their drug.

These types of medication are made to release treatment slowly to help have more even control of symptoms throughout the day.

Each heading identifies the class of drug used to treat Parkinson's disease, such as levodopa or dopamine agonists (Fig. 1.5). In bulleted lists, the unbranded name is listed first, followed by the branded name in bold. For example, the pharmaceutical company Roche uses the brand name Madopar to market co-

beneldopa medicines.

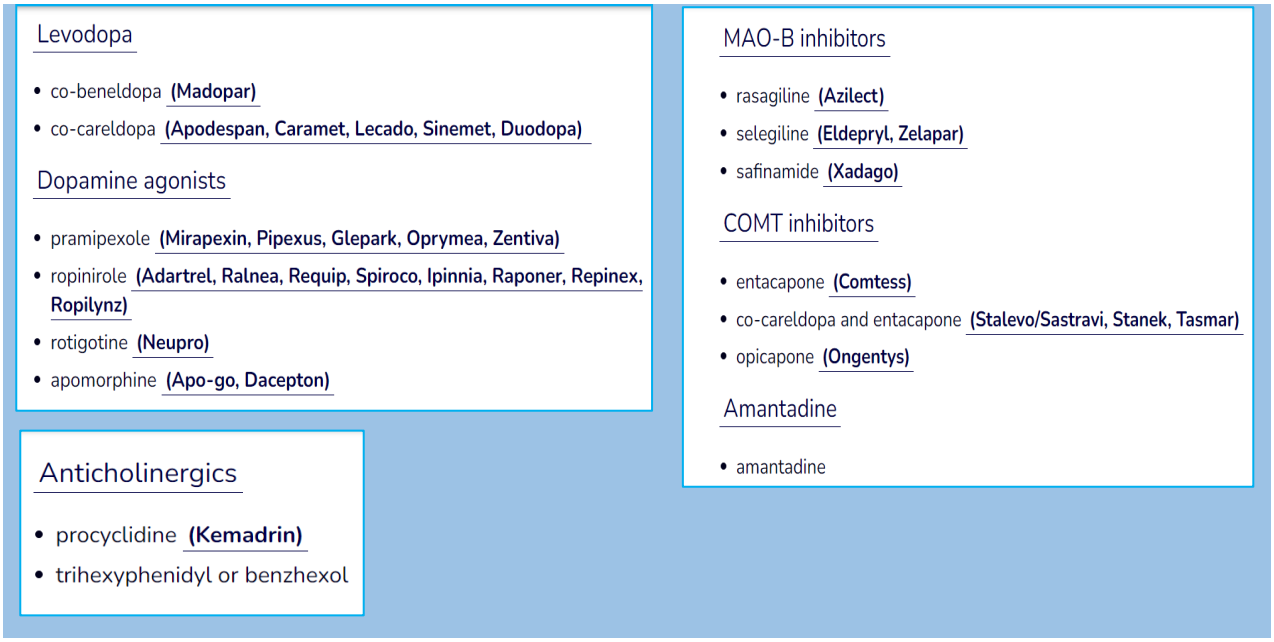

Fig. 1.5. Parkinson's drugs

Levodopa (co-beneldopa and co-careldopa)

Co-beneldopa (benserazide and levodopa)

- ✓ Madopar (capsules, dispersible tablets)
- ✓ Madopar CR (controlled release capsules)

Co-careldopa (carbidopa and levodopa)

- ✓ Apodespan PR (prolonged release tablets)
- ✓ Caramet CR (controlled released tablets)
- ✓ Lecado (modified release tablets)
- ✓ Half Sinemet CR (controlled release tablets)
- ✓ Sinemet (tablets)
- ✓ Sinemet Plus (tablets)
- ✓ Sinemet CR (controlled release tablets)
- ✓ Duodopa (intestinal gel)

Co-careldopa (carbidopa and levodopa) and entacapone

- ✓ Stalevo (tablets)
- ✓ Sastravi (tablets)
- ✓ Stanek (tablets)

Levodopa is a precursor to dopamine, a neurotransmitter that plays a role in movement, mood, and cognition. Carbidopa is a peripheral decarboxylase inhibitor that prevents the breakdown of levodopa in the body. When levodopa and carbidopa are taken together, they increase the amount of levodopa that reaches the brain, where it can be converted to dopamine and relieve the symptoms of Parkinson's disease [2-4, 17, 18].

The mechanism of action of levodopa and carbidopa is as follows [2-4]:

- Levodopa is taken orally and absorbed into the bloodstream.
- Levodopa is transported to the brain by a protein called L-amino acid decarboxylase.
- In the brain, levodopa is converted to dopamine by the enzyme aromatic L-amino acid decarboxylase.
- Dopamine binds to dopamine receptors in the brain and activates them.
- Activation of dopamine receptors produces the beneficial effects of levodopa, such as improved movement, mood, and cognition.

A peripheral decarboxylase inhibitor called carbidopa stops the body from decomposing levodopa. This is significant since the enzyme aromatic L-amino acid decarboxylase also breaks down levodopa in the body. Levodopa is turned into dopamine more readily in the brain when carbidopa inhibits this enzyme.

Levodopa and carbidopa together are a highly successful Parkinson's disease medication [2-4, 31-33]. In those with Parkinson's disease, it can enhance cognition, mood, and movement. Levodopa and carbidopa, however, can also have undesirable side effects such as dyskinesia (uncontrolled movement), nausea, and vomiting.

Pharmacodynamic effects of levodopa and carbidopa [2-4]

The pharmacodynamic effects of levodopa and carbidopa are complex and involve a number of different mechanisms. Dopamine, a neurotransmitter involved in movement, mood, and cognition, is a precursor to levodopa. The enzyme aromatic L-amino acid decarboxylase converts levodopa into dopamine once it reaches the brain. The brain's dopamine receptors are then activated as a result of dopamine's

binding to them. The advantages of levodopa include better movement, mood, and cognition because dopamine receptors are activated. A peripheral decarboxylase inhibitor called carbidopa stops the body from decomposing levodopa. This is significant since the enzyme aromatic L-amino acid decarboxylase also breaks down levodopa in the body. Levodopa is turned into dopamine more readily in the brain when carbidopa inhibits this enzyme. Levodopa and carbidopa together are a highly successful Parkinson's disease medication. In those with Parkinson's disease, it can enhance cognition, mood, and movement. Levodopa and carbidopa, however, can also have undesirable side effects such dyskinesia (uncontrolled movement), nausea, and vomiting [32, 33].

The following are some of the pharmacodynamic effects of levodopa and carbidopa [2-4]:

✓ Improved movement – levodopa and carbidopa can improve movement in people with Parkinson's disease by increasing the levels of dopamine in the brain. Dopamine is a neurotransmitter that plays a role in movement, so increasing its levels can help to improve movement problems.

✓ Improved mood – levodopa and carbidopa can improve mood in people with Parkinson's disease by increasing the levels of dopamine in the brain. Dopamine is also involved in mood regulation, so increasing its levels can help to improve mood.

✓ Improved cognition – levodopa and carbidopa can improve cognition in people with Parkinson's disease by increasing the levels of dopamine in the brain. Dopamine is also involved in cognitive function, so increasing its levels can help to improve cognition.

✓ Nausea and vomiting – levodopa and carbidopa can cause nausea and vomiting in some people. This is because levodopa can stimulate the vomiting center in the brain.

✓ Dyskinesia – levodopa and carbidopa can cause dyskinesia (uncontrolled movements) in some people. This is because levodopa can overstimulate dopamine

receptors in the brain.

Features of pharmacokinetics of levodopa and carbidopa [2-4]

Levodopa and carbidopa's pharmacokinetics are intricate and involve numerous variables. Levodopa and carbidopa's pharmacokinetics have several important characteristics, some of which are:

✓ Absorption – levodopa is absorbed rapidly from the gastrointestinal tract. The peak plasma concentration of levodopa is reached within 1 to 2 hours after oral administration.

✓ Distribution – levodopa is widely distributed throughout the body. It crosses the blood-brain barrier and is concentrated in the brain.

✓ Metabolism – levodopa is metabolized in the liver by the enzyme aromatic L-amino acid decarboxylase. Carbidopa also inhibits this enzyme, which helps to increase the amount of levodopa that reaches the brain.

✓ Excretion – levodopa is excreted in the urine. The half-life of levodopa is about 2 hours.

The pharmacokinetics of levodopa and carbidopa can be affected by a number of factors, including [2-4]:

- Age – the pharmacokinetics of levodopa and carbidopa may be altered in older adults.
- Diet – the pharmacokinetics of levodopa and carbidopa may be affected by the intake of protein. Protein can block the absorption of levodopa, so it is important to take levodopa and carbidopa at least 30 minutes before or after meals.
- Other medications – levodopa and carbidopa may interact with other medications. It is important to talk to your doctor about all of the medications you are taking before starting levodopa and carbidopa.

Side effects of levodopa and carbidopa

✓ Nausea and vomiting

✓ Dizziness and lightheadedness

✓ Motor fluctuations, wearing off and dyskinesia

Being «on» or «off» is different from being «freezing». If a person's symptoms are well controlled, this is called an «on» period, which means the medication is working well. When symptoms return, this is called a «off» period. This may mean that a person who has gone for a walk suddenly cannot continue walking or, while sitting, cannot get up to open the door. «Off» periods usually come on gradually, but can sometimes be more sudden. When they appear suddenly, some people compare this «on/off» effect to turning a light switch on and off. But when a person freezes, it only affects certain movements. For example, they may not be able to walk, but they can still reach for a cup. Freezing can be described by people as feeling as feet are «glued» to the ground [31, 32].

- ✓ Mental changes (hallucinations or delusions)
- ✓ Impulsive and compulsive behavior
- ✓ Sleep problems (insomnia and restless legs syndrome)
- ✓ Other side effects (constipation, dry mouth, and changes in blood pressure).

Combining two or more medications to treat a condition is known as drug therapy. It is a standard procedure in medicine and has the potential to significantly enhance the effectiveness and safety of care [2-4].

The following guiding principles apply to the usage of medication combinations [2-4]:

- ✓ Selecting the right drugs

The first step in drug combination is to select the right drugs. The drugs should be chosen based on their mechanism of action, their side effect profile, and their potential for interactions.

- ✓ Considering the patient's overall health

It is also important to consider the patient's overall health when selecting drugs for combination therapy. The patient's age, weight, liver and kidney function, and other medical conditions should all be taken into account.

- ✓ Starting with low doses

When starting drug combination therapy, it is important to start with low doses. This will help to minimize the risk of side effects. The doses can then be gradually increased as needed.

✓ Monitoring for side effects

It is important to monitor patients closely for side effects when they are taking drug combination therapy. Side effects can be more common when multiple drugs are used together.

✓ Adjusting the dose

If side effects occur, the dose of one or more of the drugs may need to be adjusted. It is important to work with the doctor to find the best dose for each patient [36, 37].

Combining medications to treat a condition can be highly successful [2-4, 33]. To ensure a safe and successful medicine combination, it is crucial to adhere to certain rules.

The following are a few advantages of medication combinations [2-4, 33]:

- Improved efficacy

Drug combination can often improve the efficacy of treatment. This is because the drugs can work together to target the disease in different ways.

- Reduced side effects

Drug combination can also help to reduce side effects. This is because the drugs can work together to reduce the amount of each drug that needs to be used.

- More convenient

Drug combination can often be more convenient for patients. This is because it can reduce the number of pills that need to be taken each day.

Here are some of the risks of drug combination [2-4]:

✓ Increased side effects

Drug combination can increase the risk of side effects. This is because the drugs can interact with each other and cause unexpected side effects.

✓ Drug interactions

Drug combination can also increase the risk of drug interactions. This is because the drugs can interact with each other and change the way they work.

✓ Ineffectiveness

Drug combination can sometimes be ineffective. This is because the drugs may not work together to target the disease in the right way.

1.4. Prospects for the development of a new delivery platform to improve the pharmacokinetics and therapeutic effect of complex drugs containing a combination of levodopa and carbidopa

For some people with PD, protein (which is found mainly in meat, fish, eggs, cheese, beans, and pulses) seems to interfere with how well levodopa medications are absorbed by the body. Because of this, it may benefit from taking the medication 30-60 minutes before eating. It may also benefit from a protein redistribution diet, where patients take most of their daily protein in the evening. This can help the levodopa treatment to be more effective in the daytime when patients are likely to need it more. PD causes progressive disability that can be slowed but not halted by treatment. Therefore, the goal of medical management of PD is to control the signs and symptoms of the disease for as long as possible while minimizing adverse effects. The challenge in maintaining LD plasma levels within this progressively narrowing therapeutic window is complicated by LD's narrow absorption window, with absorption limited to the upper GI tract, as well as LD's short clearance half-life when taken with CD. As high levels of LD are associated with dyskinesia development, it is preferable to maintain peak LD levels just high enough for efficiency. Reducing LD dosage while maintaining stable LD levels should help patients with PD maintain more consistent motor function [1-4].

Duodopa® (Fig. 1.6) [2-4, 34, 35]

LD-CD intestinal gel (LD-CD IG) – Duodopa – is a gel form of LD (co-careldopa) reserved for advanced and complex Parkinson's. It is pumped through a

tube that is surgically inserted into the intestine. This means the dose of medication acts more quickly. LD-CD IG can help reduce involuntary movements as a side effect of medication, reduction in off'-time (motor fluctuations from drugs wearing off), and problems with symptoms at night. LD-CD IG is only suitable for a few people whose symptoms can’t be controlled with more common drug treatments, such as levodopa tablets. Most frequent adverse events were related to the procedure or the device [34, 35].

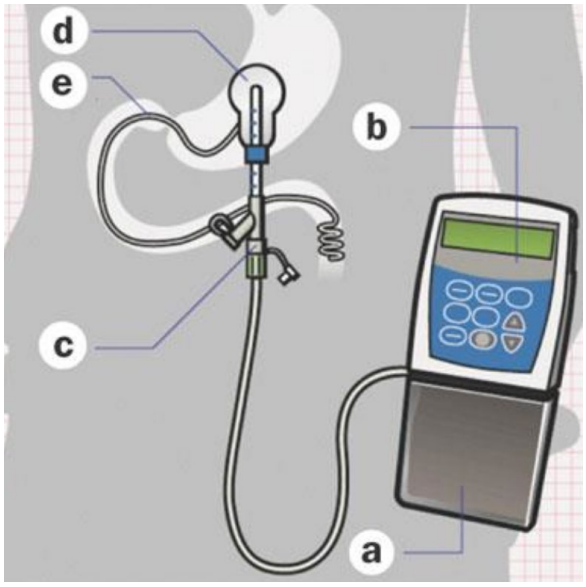

Fig. 1.6. Duodopa® intestinal infusion system

Notes:

1) A – cassette with duodopa
2) B – pump
3) C – gastrojejunostomy tube
4) D – stoma
5) E – intestinal tube

Levodopa duodenal infusions have been demonstrated to provide significantly more constant plasma concentrations and to significantly lessen motor fluctuations in Parkinson's disease patients, including when compared with oral carbidopa-levodopa for immediate release and controlled release.

Patients with severe Parkinson's disease typically get a 16-hour infusion of

levodopa-carbidopa intestinal gel (LCIG; also known as carbidopa-levodopa enteral solution), however clinical findings indicate that a 24-hour infusion may further improve symptoms. This evaluation offers helpful guidance on how to handle patients switching to a 24-hour LCIG infusion. Based on our clinical experience, we address dosage modifications, suggestions for monitoring, and the management of patient concerns after reviewing the available clinical data for 24-hour infusion. Multiple studies' worth of data indicate that LCIG might help non-motor symptoms. Although few studies have looked at 24-hour LCIG infusion, the information that is currently available suggests that certain patients may benefit from round-the-clock care. Small sample sizes and open-label study designs restrict studies of 24-hour LCIG infusion, It can make it difficult to translate to clinical practice. In our experience, patients may gain from a 24-hour infusion when nocturnal symptom reduction and sleep quality enhancement are desired. A patient may potentially benefit from a 24-hour infusion if their freezing of gait while taking levodopa is unresponsive, or if their problematic dyskinesias are not adequately controlled. As with 16-hour infusion, patients should be watched for autonomic dysfunction, overnight wearing off symptoms, weight changes, fluctuations in plasma levels of vitamins B_6/B_{12}, folate, and homocysteine, changes in sleep patterns, and dose adjustments, particularly of the nocturnal rate, or a worsening of nightmares, hallucinations, or delusions. A 24-hour LCIG regimen may be necessary for some patients with poorly controlled nighttime variations or early morning «off» symptoms, according to the available research and our clinical experience [32–35].

Accordion Pill™ (Fig. 1.7) [2-4]

The Accordion Pill™ (AP) represents a novel gastric-retention oral delivery platform based on folded multilayer films (Intec Pharma, Jerusalem, Israel) to enhance pharmacokinetics (PK) and therapeutic benefit of challenging drugs. AP is characterized by one or more of the following: narrow absorption window (poor colonic absorption), narrow therapeutic window (maximum plasma concentrations correlate with adverse events and/or trough levels correlate with poor efficiency), poor solubility (low solubility, high permeability (Biopharmaceutics Classification

System (BCS) class II) and low solubility, low permeability (BCS class IV) and act locally, in the stomach or in the upper part of the GI tract. Furthermore, AP allows multiple drug release profiles in a single capsule and can provide fixed-dose combinations.

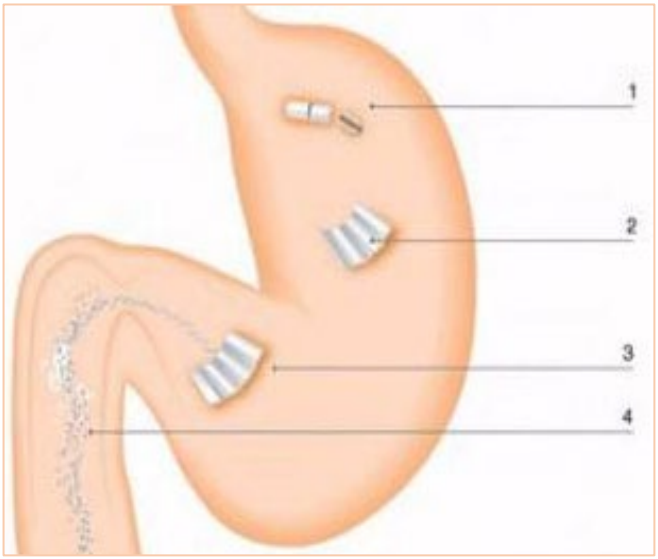

Fig. 1.7. The Accordion Pill®

Phase II clinical trials (CT) have evaluated gastric retention and PK of AP in healthy volunteers and the efficacy and safety of AP-containing CD-LD (AP-CD-LD) in PD patients. AP was retained in the stomach for approximately 8 h, without special meal requirements. AP-CD-LD demonstrated improved absorption, more stable levodopa exposure, and improved time compared with immediate-release CD-LD in advanced PD patients. AP-CD-LD may achieve stable LD plasma concentrations with significantly fewer daily doses. Despite potential problems with intestinal motility, earlier clinical trials demonstrated that PD patients retained the AP for 11.8–13.9 h. AP-CD-LD consists of five layers with both immediate release and controlled release components for CD-LD fixed-dose combination. As high levels of LD are associated with the development of dyskinesia and deep troughs in LD availability are associated with pulsatile stimulation of dopamine receptors in the striatum, the results observed with AP-CD-LD are promising for providing efficiency while reducing risks of motor complications. AP-CD-LD is currently in Phase III clinical trials: a multi-center, global, randomized, double-blind, double-

dummy, active-controlled, parallel-group study in adult subjects with fluctuating PD – A Study to Assess the Safety and Efficacy of the Gastric-retentive AP-CD-LD in Advanced Parkinson's Patients (Accordion Pill™, Sinemet®, Placebo-AP-CD-LD, and Placebo- Sinemet). In patients with advanced PD, AP technology showed efficient controlled-release PK performance and decreased motor response variations. Currently, a phase 3 randomized controlled CT is being conducted [2-4].

NEUPRO® (Fig. 1.8) [2-4]

NEUPRO® Rotigotine Transdermal System Can be used at any stage of Parkinson's disease alone, with levodopa or with other drugs. A new patch should be applied at the same time every day. May cause skin irritation, do not reapply to the same area for at least 14 days.

Fig. 1.8. NEUPRO® Rotigotine Transdermal System

Continuous delivery of LD-CD IG offers a promising option for the control of advanced Parkinson's disease with motor complications. AP-CD-LD, with its controlled release and gastric retentive formulation, has demonstrated improved efficacy and safety in early clinical trials in patients with advanced PD, with a significant reduction in daily dosing. Pharmacists can help patients understand the medication they are prescribed and explain how to take it. If the patient has other illnesses or conditions and needs medication, the pharmacist can guide him/her on how to take these alongside Parkinson’s medication. It is useful to keep the

packaging for medication. This will help the patient to remember what the patient is taking. The patient can also record the name and strength of the medication and carry this list with him/her for when the patient needs it. This will be particularly useful in an emergency, as it will help medical professionals to understand what medication the patient takes

Conclusions for Chapter 1

1) According to the results of the literature review, Parkinson's disease is one of the most common degenerative diseases in the elderly. Parkinson's disease requires financial costs from both the state and the patient.

2) The most frequently prescribed group of drugs is a combination of a dopamine precursor (levodopa) and a decarboxylase inhibitor (carbidopa). Wide use of this class of drugs is based on a combination of their high efficiency, good tolerability, and safety.

3) Carbidopa-levodopa enteral suspension safely and effectively treats motor and some non-motor features of Parkinson's disease, leading to improved quality of life and reduced off-time without worsening troublesome dyskinesia. Continual infusions throughout the day provide patients with more predictable motor function, reflecting the more stable plasma levels of levodopa shown with this therapy. Safety concerns revolve around the procedure for tube placement and complications of the device. Centers offering this therapy must be prepared to manage and overcome device complications as they arise.

5) Overall, carbidopa-levodopa enteral suspension provides a meaningful alternative for advanced PD patients who suffer from motor fluctuations that cannot be adequately managed with oral and other less invasive medications.

4) If long-term use of drugs is necessary, it is important that the doctor and the patient and/or caregivers observe the correct administration of the drug (before, during, after meals), the intervals between taking Parkinson's drugs and food, and how to discuss possible side effects of drugs.

CHAPTER 2

MATERIALS AND METHODS

The study's practical component was carried out in collaboration with Al-jammal and Medany Pharmacies in Ismailia, Egypt. The questionnaires, which we created in two versions and are shown in Figures 2.1 and 2.2, are as follows:

1) A questionnaire for pharmacists about awareness of intestinal gel containing levodopa and carbidopa use for Parkinson's disease treatment.

2) A survey to see if customers of pharmacies are aware of the proper usage of levodopa-carbidopa oral medications for treating Parkinson's disease.

We analyzed most questions of pharmacists and other questions of pharmacy visitors on their awareness of the rational use of intestinal gel and levodopa-carbidopa oral medications for treating Parkinson's disease and the criteria of effectiveness and safety of treatment. Two different versions of the questionnaire were used to conduct the survey. There were written questions as well as assessments on the internet. Both pharmacists and customers of pharmacies can choose which version of the questionnaire is most practical for them.

Statistical analysis of the results was performed using a one-way Kruskal-Wallis analysis of variance and the Mann-Whitney test for posterior pairwise comparisons [38, 39]. The computer software used included IBM SPSS STATISTICS V. 22 (IBM Corp., USA) and ms EXCEL 2016 (Microsoft Corp., USA). The level of statistical significance was considered $p < 0.05$ [40].

QUESTIONNAIRE FOR PHARMACIST

about awareness of intestinal gel containing levodopa and carbidopa use for Parkinson's disease treatment

To fill in the questionnaire, circle the correct answers or write the necessary information by hand.

Thank you for your cooperation!

Do you know the clinical forms of Parkinson`s disease?

☐ Yes ☐ No ☐ I don't have precise information

1.

2.

Do you know the pharmacological groups of drugs used to Parkinson's disease treatment?

☐ Yes ☐ No ☐ I don't have precise information

1.

2.

What are the general rules for using levodopa-carbidopa intestinal gel for t Parkinson's disease treatment?

1.

2.

What are the advantages/disadvantages of levodopa-carbidopa intestinal gel for Parkinson's disease treatment? If you know, enter the trade name.

I don’t have enough information

1.

2.

What criteria for choosing levodopa-carbidopa intestinal gel do you know? Indicate the degree of importance.

I don’t have enough information

1.

2.

What side effects of levodopa-carbidopa intestinal gel do you know and have you informed the consumer about these risks?

1.

2.

Fig. 2.1. Version of the questionnaire for pharmacists about awareness of intestinal gel containing levodopa and carbidopa use for Parkinson's disease treatment

QUESTIONNAIRE FOR PHARMACY VISITOR

about awareness of the rational use of levodopa-carbidopa oral drugs for Parkinson's disease treatment

To fill in the questionnaire, circle the correct answers or write the necessary information by hand.

Thank you for your cooperation!

Write some general rules for using oral drugs.

1.
2.
3.

Have you been told by your doctor and/or pharmacist about the potential side effects of levodopa-carbidopa oral drugs? If so, name these side effects.

☐ Yes ☐ No ☐ I don't have the precise information

1.
2.
3.

Have you been informed by your doctor and/or pharmacist about the rules for the rational use of levodopa-carbidopa oral drugs? If so, provide this information.

☐ Yes ☐ No ☐ I don't have the precise information

1.
2.
3.

Fig. 2.2. Version of the questionnaire for pharmacy visitors about their awareness of the rational use of levodopa-carbidopa oral drugs for Parkinson's disease treatment

Conclusion for Chapter 2

The questions about treatment efficiency criteria and factors that are most essential from the patient's point of view for treatment efficacy were the same in both questionnaires. The questions and answers were used in the patient questionnaire to help patients comprehend. To obtain optimal therapeutic outcomes

while managing potential side effects, the sensible use of levodopa-carbidopa oral medicines entails personalized and customized treatment, adherence to specified recommendations, and regular monitoring. Throughout the patient`s treatment journey, his medical professional is the patient`s best resource for personalized information and counselling and my role is to help the patient to knows everything about the drug he`s taking from my pharmacy and provide him with enough information he needs.

CHAPTER 3

STUDY RESULTS AND PRACTICAL RECOMMENDATIONS

3.1. The pharmacists' survey results regarding their awareness of intestinal gel containing levodopa and carbidopa use for Parkinson's disease treatment

We analyzed questionnaires from 29 pharmacists on their awareness of intestinal gel containing levodopa and carbidopa use for Parkinson's disease treatment. Survey results are presented below

First, we have to knows that awareness of pharmaceutical care among pharmacists plays a crucial role in ensuring optimal patient outcomes. Pharmacists who are knowledgeable about the specific characteristics, indications, and potential side effects of medications like levodopa and carbidopa can provide valuable guidance to patients and contribute to their overall treatment plan.

After analyzing most questions of pharmacists and other questions of pharmacy visitors on their awareness of the rational use of intestinal gel and levodopa-carbidopa oral medications for treating Parkinson's disease and the criteria of effectiveness and safety of treatment.

In response to the question «Do you know the clinical forms of Parkinson`s disease? Name them» 70% of respondents answered «yes», 10% answered «no» and 20% of all respondents considered this information irrelevant.

When answering the question «Do you know the pharmacological groups of drugs used to treat PD? Name them» answers were distributed as follows (by frequency) (Fig. 3.1):

1) monoamine oxidase type B (MAO B) inhibitors. (53%);
2) Dopamine agonists (25%);
3) The catechol-O-methyl transferase (COMT) inhibitors (14%);
4) Others (8%), in that case – anticholinergic, Amantadine, Istradefylline.

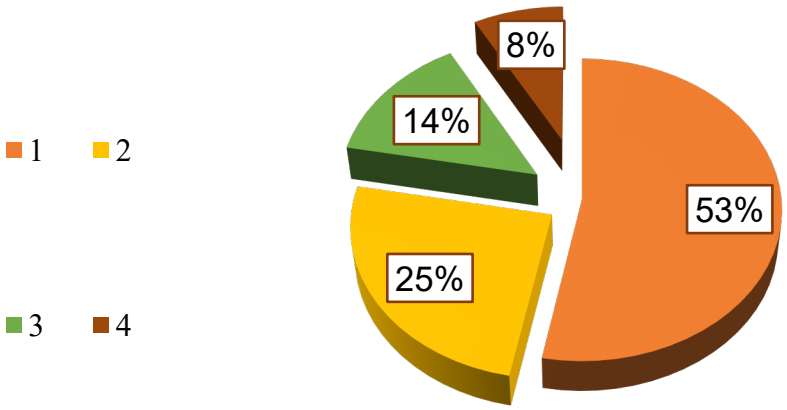

Fig. 3.1. «Do you know the pharmacological groups of drugs used to treat PD? Name them»

Answering the question «Write some general rules for using levodopa-carbidopa intestinal gel for treating PD?» respondents' answers were distributed as follows (by frequency of recommendations) (Fig. 3.2):

1) Patient selection (35%)

Advanced PD patients who exhibit dyskinesias and motor fluctuations that are difficult to control with oral medicines are frequently candidates for LCIG. It is typically started after other treatments, such as deep brain stimulation or oral medicines, are no longer effective at relieving symptoms.

2) Administration (18%)

A portable pump apparatus that distributes the drug via a tube (intestinal tube) directly into the small intestine is used to administer LCIG. Percutaneous endoscopic gastrojejunostomy (PEG-J), a surgical treatment, is used to place the tube. This procedure entails putting the tube in the stomach and advancing it into the jejunum, a section of the small intestine.

3) Individualized dosing (40%)

Depending on each person's unique symptoms and reaction to the medicine, the dosage of LCIG is adjusted to meet their needs. Healthcare practitioners modify the dosage to maximize symptom control while minimizing negative effects. It is

crucial to strictly adhere to the suggested dose schedule and any modifications suggested by the medical staff.

4) Monitoring and Follow-up (7%)

When utilizing LCIG, routine monitoring and follow-up consultations are required. This aids medical personnel in evaluating the efficacy of the therapy, modifying the amount of the medicine as needed, and addressing any issues or adverse effects that could emerge.

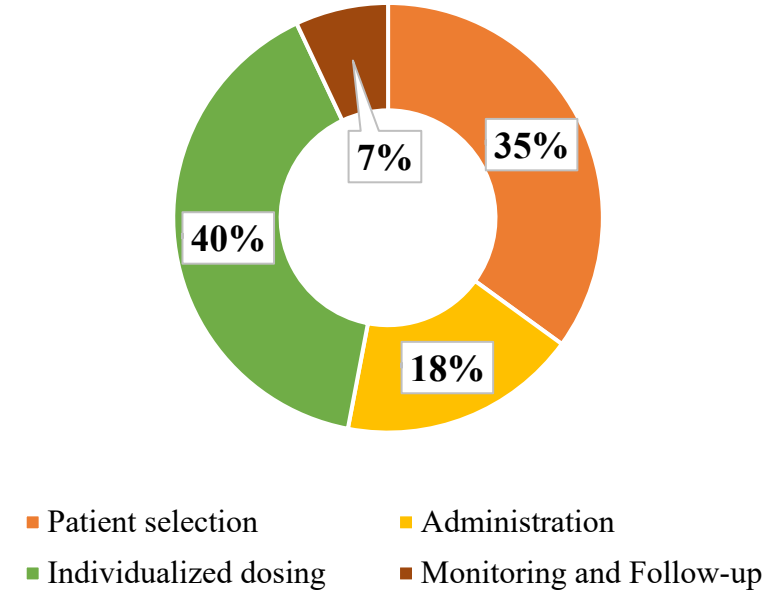

Fig. 3.2. «Write some general rules for using levodopa-carbidopa intestinal gel for treating PD?»

Answering the question «What side effects of LCIG do you know and have you informed the consumer about these risks?».

Of corse I should inform the patient about the risks of LCIG but also it's important to note that not everyone will experience these side effects, and their severity can vary among individuals. It's crucial to discuss any concerns or side effects with the healthcare provider overseeing the LCIG treatment. They can provide appropriate guidance, adjust the medication regimen if needed, and help manage side effects to optimize the benefits of the therapy.

1. Vomiting and nausea

LCIG treatment frequently causes gastrointestinal adverse effects, such as nausea and vomiting. These side effects may appear at the beginning of therapy or after dosage modifications. To help control these symptoms, additional drugs or changes to the treatment schedule may be advised.

2. Abdominal discomfort and cramping

A side effect of LCIG for some people may be abdominal discomfort and cramping. It's crucial to alert the medical staff if these symptoms appear so they can assess the situation and maybe change the medication's dosage.

3. Orthostatic hypotension

LCIG can lower blood pressure when you stand up, which might make you feel faint, woozy, or dizzy. Orthostatic hypotension is what is meant by this. To manage this adverse effect, proper blood pressure monitoring, medication adjustments, or lifestyle changes may be advised.

4) Dyskinesias

Involuntary movements that can happen as a result of long-term levodopa use, particularly LCIG, are known as dyskinesias. Dyskinesias can cause jerky, twisting, or writhing motions. To reduce these uncontrollable movements while still maintaining symptom control, changes to the pharmaceutical regimen may be required.

5) Some people on LCIG may develop hallucinations, which entail hearing or seeing things that are not actually there. Additionally, psychiatric side effects such disorientation, agitation, and mood swings might happen. It's critical to let the healthcare practitioner know if your mood or cognitive change.

6) LCIG can lead to sleep disturbances such as insomnia, vivid nightmares, or even excessive daytime sleepiness. The medical professional should be informed of these side effects in order to evaluate them and maybe make adjustments to the patient's prescription or sleep hygiene techniques.

7) Skin issues

Some people who use LCIG may develop skin issues at the place where the PEG-J tube is implanted. Redness, discomfort, infection, or leakage around the tube

are examples of these. To reduce the possibility of problems, proper care, hygiene, and regular monitoring of the insertion site are required.

3.2. The pharmacy visitors' survey results regarding their awareness of the rational use of levodopa-carbidopa oral drugs for Parkinson's disease treatment

Pharmacists are trusted health experts who must advise and educate patients, therefore PD management begins in pharmacies. The pharmacist should be able to recognize Parkinson's disease symptoms, assess the severity of the patient's symptoms, and decide whether to refer the patient to a doctor. The pharmacist should be able to select the best medication for the patient based on his symptoms and evaluate whether it is possible to offer the patient vitamins to enhance his health. Nausea and vomiting, dyskinesias, orthostatic hypotension, hallucinations and delusions, sleep difficulties, and impulse control disorders are all symptoms of Parkinson's disease. Constipation, dry mouth, dizziness, headache, confusion, anxiety, or mood disturbances are all possible side effects of levodopa-carbidopa. Notify your doctor if any of these side effects are troublesome or persistent. If the patient has unilateral symptoms, unsteady blood pressure, high or low glucose levels in the blood, any neurological disease, pain, recurring nosebleeds, or olfactory loss, he should see a doctor and should not take over-the-counter drugs. Patients should also see a doctor if they are pregnant, have shortness of breath, are on any drugs that may trigger symptoms or do not react to over-the-counter medication. As with any new prescription drug, the patient should be instructed on any over-the-counter product and told how important it is to stick to the regimen. The patient should be told when to expect symptom relief.

We analyzed 71 questionnaires from pharmacy visitors on their awareness of the rational use of levodopa-carbidopa oral drugs for Parkinson's disease treatment. Survey results are presented below.

When the surveys of pharmacy visitors were examined, it was discovered that

a majority of them (35%) could identify at least one rule for taking levodopa/carbidopa 250/25. «Follow the instructions for use» (20%) was the most popular response. Approximately half of the respondents (45%) were warned about the potential side effects of levodopa/carbidopa 250/25 by both the doctor and the chemist. Nausea and vomiting, dyskinesias, hallucinations and delusions, sleep problems, and impulse control issues were the most commonly anticipated side effects (70%).

When answering the question «Have you been told by your doctor and/or pharmacist about the potential side effects of levodopa-carbidopa 250/25 oral drugs? If so, name these side effects.» the answers were distributed as follows:

- 68% answered «Yes, informed by the doctor about side effects»;
- 20% answered «Yes, informed the pharmacist about the sequences of not taking the drug in time»;
- 12% out of all respondents consider this information irrelevant.

And when answering the question «Have you been informed by your doctor and/or pharmacist about the rules for the rational use of levodopa-carbidopa oral drugs?» If so, provide this information.

- 80% answered «Yes», informed by the doctor about the rules for the rational use of the drug and the dosage forms;
- 15% answered «Yes», informed the pharmacist about the dosage form and how to take the drug with eating;
- 5% answered «no», the had no idea because they are newly taking this type of drug or they were taking another drug and just changed to this new one.

Pharmacists are trusted health experts who must advise and educate patients, therefore PD management begins in pharmacies. The pharmacist should be able to recognize Parkinson's disease symptoms, assess the severity of the patient's symptoms, and decide whether to refer the patient to a doctor. The pharmacist should be able to select the best medication for the patient based on his symptoms and evaluate whether it is possible to offer the patient vitamins to enhance his health.

Nausea and vomiting, dyskinesias, orthostatic hypotension, hallucinations and delusions, sleep difficulties, and impulse control disorders are all symptoms of Parkinson's disease. Constipation, dry mouth, dizziness, headache, confusion, anxiety, or mood disturbances are all possible side effects of levodopa-carbidopa. Notify your doctor if any of these side effects are troublesome or persistent. If the patient has unilateral symptoms, unsteady blood pressure, high or low glucose levels in the blood, any neurological disease, pain, recurring nosebleeds, or olfactory loss, he should see a doctor and should not take over-the-counter drugs. Patients should also see a doctor if they are pregnant, have shortness of breath, are on any drugs that may trigger symptoms or do not react to over-the-counter medication. As with any new prescription drug, the patient should be instructed on any over-the-counter product and told how important it is to stick to the regimen. The patient should be told when to expect symptom relief.

Patients should be urged to continue taking the medication as advised in order to receive the best possible symptom alleviation. Improper administration can also result in decreased efficacy because the patient does not receive the entire required dose. It is critical that patients understand the most prevalent side effects and when they must notify their doctor. Patients should also be taught how to read product labels and understand the active substances. By boosting patient compliance with health issues, proper patient education and counseling can help optimize patient treatment. The chemist plays an important role in the detection of undetected or untreated diseases, as well as in strengthening cooperation among all healthcare providers to ensure optimal patient treatment. Additionally, the chemist should provide the patient with general instructions on how to use the drug, such as:

1. Follow the dose instructions: Take the medication exactly as directed by your healthcare practitioner. The dosage will depend on your specific demands, symptoms, and medical history.

2. Timing of doses: Levodopa and carbidopa are usually taken multiple times a day, as directed by your healthcare provider. It's important to follow the prescribed schedule and maintain a consistent dosing routine to ensure optimal effectiveness.

3. Take with or without food: Levodopa and carbidopa can be taken with or without food. However, taking the medication on an empty stomach, typically 30 minutes before meals or 1 hour after meals, may help improve absorption.

3.3. Practical recommendations for pharmacists and visitors to pharmacies / patients / caregivers on the specifics of pharmaceutical care when using levodopa and carbidopa in the treatment of Parkinson's

Compliance between the patient and the doctor/pharmacist is an important component in the treatment of PD. The recommendations are aimed at improving the quality of life of PD patients. Taking into account the side effects of Parkinson's drugs and the specifics of their use, we decided to develop a diary for patients, which consists of certain sections and where certain questions will be asked, in order to choose a rational and effective treatment for Parkinson's drugs:

✓ Do you have the following psychotic symptoms: hallucinations and delusional disorders? (related to the treatment of CP, the risk of which increases with the appointment of dopamine agonists);

✓ Does daytime sleepiness bother you?;

✓ How often do you go to the restroom? (How many times a day? Do you observe stool problems (constipation)?;

✓ In what period of time do you consume protein food?

✓ Do you follow the recommendations for dividing the levodopa tablet into 4–5 doses?

First of all, I want to remind you about my duties as a pharmacist.

As a pharmacist, my primary role is to ensure the safe and effective use of medications for patients. I have a diverse range of responsibilities that revolve around medication management, patient care, and healthcare collaboration. Here are some key duties I would perform as a pharmacist:

I. Dispensing medications

One of my main tasks is to accurately interpret prescriptions and dispense the

appropriate medications to patients. I ensure that the right dosage and instructions are provided, taking into account factors such as drug interactions and patient allergies.

II. Patient consultations

I play an important role in counseling patients about their medications. I educate them on proper medication use, potential side effects, and precautions to take. I address any questions or concerns they may have and offer advice on maintaining a healthy lifestyle.

III. Medication review

I conduct thorough medication reviews to ensure that patients are on appropriate drug therapies. This involves assessing medication regimens, checking for duplicate therapies or interactions, and making recommendations to optimize treatment outcomes. I collaborate with healthcare providers to make any necessary adjustments.

IV. Medication safety

Patient safety is paramount, and I take steps to prevent medication errors. I verify the accuracy of prescriptions, check for potential contraindications, and employ proper labeling and storage practices. I may also provide guidance on the safe disposal of medications.

V. Adverse event monitoring

I monitor and report adverse drug reactions or medication errors to the relevant authorities. This helps to identify potential issues with medications and contributes to pharmacovigilance efforts to improve patient safety.

VI. Drug information

I serve as a reliable source of drug information for healthcare professionals and patients. I stay updated on the latest research, drug interactions, and emerging therapies. I provide evidence-based recommendations and collaborate with other healthcare team members to optimize patient care.

VII. Health promotion

As a pharmacist, I actively promote health and disease prevention. I may offer

immunizations, conduct health screenings, and provide guidance on lifestyle modifications, such as smoking cessation, weight management, and medication adherence.

VIII. Collaborative care

I work closely with physicians, nurses, and other healthcare professionals to ensure comprehensive and coordinated patient care. I participate in interdisciplinary teams, sharing my expertise and contributing to treatment plans.

IX. Pharmacy management

In addition to direct patient care, pharmacists may also have administrative responsibilities. This includes managing inventory, ensuring compliance with regulations and standards, overseeing pharmacy operations, and mentoring pharmacy students or interns.

Overall, as a pharmacist, I strive to optimize medication therapy, promote patient well-being, and ensure medication safety through effective communication, education, and collaboration within the healthcare team.

In our case of practice recommendations about the specifics of pharmaceutical care when taking immediate-release levodopa and carbidopa 250/25 mg in Parkinson's disease treatment.

First, I should give a short note about the drug and its medical benefit and how it works:

Levodopa/carbidopa is an antiparkinsonian drug used to treat Parkinson's disease. Levodopa/carbidopa is a mix of two medications, namely Levodopa and Carbidopa. Levodopa is categorized as a central nervous system agent, even though carbidopa is classified as a decarboxylase inhibitor. with the brain, the pharmaceutical component Levodopa converts to dopamine, which aids with movement control. Simultaneously, Carbidopa works by reducing the breakdown of Levodopa in the bloodstream, allowing more Levodopa to enter the brain and effectively block acetylcholine (a chemical messenger in the brain).

Secondly, I should talk about the directions of use:

Take levodopa/carbidopa with or without food as advised by the patient`s

doctor. Swallow it as a whole with a glass of water. Do not crush, break or chew it, and if the patient is known to be allergic to Levodopa/carbidopa or any other medicines, he should tell his doctor. Levodopa must be discontinued at least 12 hours before starting levodopa/carbidopa. If the patient is pregnant or breastfeeding, it is advised to inform her doctor. If the patient has glaucoma, asthma, nausea, dizziness, mental illness, breathing problems, daytime sleepiness, involuntary muscle movements, intense urges like gambling, spending money, overeating, or increased sexual urges, he also should inform his doctor before taking levodopa/carbidopa.

Thirdly, we must tell the patient about the drug`s storage conditions and to Store it in a cool and dry place away from sunlight.

Fourthly, the patient must know the side effect of the drug he`s taking:

- ✓ nausea, vomiting, and loss of appetite;
- ✓ confusion;
- ✓ light-headedness;
- ✓ lowered blood pressure;
- ✓ dyskinesia (uncontrolled/involuntary muscle movement).

Fifth, drug warnings.

Patient should contact his doctor if you have a history of diabetes, heart attacks, mental illness, stomach ulcers, heart disease, or if the patient have just had a surgical treatment. It is recommended to avoid any work that requires mental alertness after taking levodopa/carbidopa. Patients on levodopa/carbidopa may also have low vitamin B12 levels and elevated methylmalonic acid levels. Aside from that, consuming levodopa/carbidopa over an extended period of time may increase the risk of neuropathy (nerve damage). In individuals with eye issues, arrhythmia, gastrointestinal bleeding, or psychosis, levodopa/carbidopa should be used with caution. If you take (MAOs or antidepressants such as dicarboxamide, phenelzine, Selegiline, or tranylcypromine, the patient should avoid using levodopa/carbidopa since it can trigger a high blood pressure (hypertension) crisis.

Sixth, we should explain to the patient about drug interaction

Drug-drug interaction

Other anti-Parkinson's medications (rasagiline, pramipexole), water pills or diuretics (furosemide), high cholesterol-lowering drugs (atorvastatin), vitamins (pyridoxine), and antipsychotic drugs (quetiapine) may interact with levodopa/carbidopa.

Drug-food interaction

Levodopa/carbidopa may interact with dietary proteins. Consuming high-protein foods such as chicken, beef, pig, eggs, and fish may impair the efficiency of levodopa/carbidopa. Unless otherwise directed by a doctor, do not combine vitamin supplements with levodopa/carbidopa. Also, avoid alcohol because it can exacerbate adverse effects like tiredness, dizziness, or difficulties concentrating.

Drug-disease interaction

Before taking levodopa/carbidopa, the patient should tell his doctor if you have glaucoma, asthma, nausea, dizziness, mental disease, breathing issues, daytime sleepiness, or involuntary muscular movements.

Eight, we should give the patient some special advice like:

✓ Do not exceed more than 1 dose (2 capsules) for any off period (recurring symptoms in between regular doses).

✓ If you have unusual urges like gambling, spending money, overeating or increased sexual urges, please inform your doctor before taking levodopa/carbidopa.

✓ Levodopa must be discontinued at least 12 hours before starting levodopa/carbidopa.

✓ Take this medication separately by as many hours as required from any iron supplements or products that are rich in iron. Intake of iron can reduce the absorption of the medication.

And for diet and life style:

✓ Drink plenty of water to avoid headaches due to dehydration.

✓ Limit the consumption of sugar-containing food or food with too many calories but fewer nutrients as it may cause tooth decay.

✓ Engage in physical activity like dancing or exercising, which will boost the metabolism and make a person more energetic.

✓ Avoid intake of alcoholic beverages with levodopa/carbidopa as it can make a person dehydrated and may affect their sleep. This can make it harder for a person's body to aid the levodopa/carbidopa in fighting off infections.

✓ It is suggested to take a light meal and avoid high-protein foods.

And finally, the patient should know that it is advised not to stop taking levodopa/carbidopa without consulting your doctor as it may lead to a severe condition called withdrawal-emergent hyperpyrexia with symptoms such as confusion, fever, muscle stiffness, changes in heartbeat and breathing. Therefore, take levodopa/carbidopa for as long as your doctor has prescribed it and if you experience any of these symptoms while taking levodopa/carbidopa, please consult your doctor so that the dose may be gradually reduced.

One of the main rules for the rational choice of PPP is diet. Due to the peculiarities of the pharmacokinetics and pharmacodynamics of levodopa, the diet is an invisible part in the treatment of CP due to the obstruction of side effects (poor digestion of protein products), it is necessary to take protein from a friend for half a day. day. One of the frequently reported side effects after taking levodopa, which requires treatment, has been recorded. For prevention, I will correct, patients need more collapse and take a carrier with sodium picosulfate or macrogol.

Patients with Parkinson's disease may find it helpful to complete the form shown in Fig. 3.3. The patient can provide details of their treatment regimen and contact details for emergencies and what help they may need. After the patient has completed the form, it is a good idea to keep this record with you and in any convenient place at home and let other people know where it is kept. It is also advisable to make photocopies for the patient, family members, and/or guardian.

When a patient visits their doctor or other healthcare provider, they often don't have enough time to talk in detail about how they feel. A diary can be an effective way to let someone know about problems the patient is experiencing, changes in condition, and how well the medication is controlling the symptoms. It can also help remind the patient of things he/she wants to discuss during the appointment with the doctor that the patient might otherwise forget.

Full name	
Date	

I am taking the following medicines (including all medicines you take, not just for Parkinson's):

Drug name *Include the trade name and international nonproprietary names*	**Dose**	**Reception time**	**The presence of «off» symptoms**	**Special requirements** *For example, do you need to take the medicine with food?*

Problems I experience when I don't get my medicine on time:	

Drugs to which I had a reaction:	

Контакт для екстрених випадків

My caregivers	
My doctor	

Fig. 3.3. A form for Parkinson's patient

The patient can also use the journal to record any uncomfortable questions that need help with but are difficult for the patient to ask about. The patient can use any type of diary or notebook. If the patient has a computer, smartphone, or tablet, he/she can keep an electronic diary. If the patient has difficulty typing, he/she can record his/her diary using a mobile phone or recording device (using video or audio). The patient himself chooses what suits him best. If the patient has a carer, it may be helpful for them to keep a diary, especially if the patient's needs are assessed together.

Conclusion for Chapter 3

1) According to the survey results, chemists' knowledge of the rules for using levodopa and carbidopa for Parkinson's disease therapy is insufficient, and some respondents (15%) do not consider this information necessary at all. This can have a negative impact on therapy efficacy. It is also worth noting the lack of disagreement (12%) on the criterion for selecting levodopa and carbidopa.

2) According to an interview of pharmacy visitors, only a small percentage (17%) were able to identify at least one rule for taking levodopa and carbidopa 250/25 mg. «Follow the instructions for use» was the most common response (13%). On the plus side, nearly half of the respondents (43%) were told about the potential adverse effects of levodopa and carbidopa by both the doctor and the chemist. Based on the findings, practical guidelines for the use of levodopa and carbidopa in the treatment of Parkinson's disease have been devised.

3) Given the foregoing, the issue of correct pharmacological care in the release of levodopa and carbidopa for Parkinson's disease treatment remains a pressing one that requires additional investigation and development.

4) By providing appropriate pharmaceutical and medical care, establishing contact with patients with CP can empower the patient to participate in treatment discussions and decisions about their care and improve the quality of life of such patients.

CONCLUSIONS

1) According to the results of the literature review, Parkinson's disease is a common disease among the central nervous system and over 8.5 million people worldwide are living with Parkinson's disease. This requires sufficient financial costs for treatment from both the State and the patient. Symptoms of Parkinson's disease can differ from person to person and nation to nation.

2) Parkinson's drugs are the basis of symptomatic treatment of Parkinson's disease. The gold standard in treatment is a combination levodopa/carbidopa 250/25 mg immediate release. There are nuances regarding the rational use of drugs containing levodopa, which should be followed in order to avoid and prevent side effects. Carbidopa-levodopa enteral suspension safely and effectively treats motor and some non-motor features of Parkinson's disease leading to improved quality of life and reduced off-time without worsening troublesome dyskinesia.

3) We developed a questionnaire to survey pharmacists about awareness of the usage of intestinal gel containing levodopa and carbidopa for treating Parkinson's disease. Based on the results of the survey, therapy is insufficient, and some respondents (15%) do not consider this information necessary at all. This can have a negative impact on therapy efficacy. It is also worth noting the lack of disagreement (12%) on the criterion for selecting levodopa and carbidopa.

4) We developed a questionnaire to survey pharmacy customers about awareness of the rational use levodopa-carbidopa oral drugs for for treating Parkinson's disease. Based on the results of the survey, only a small percentage (17%) were able to identify at least one rule for taking the levodopa and carbidopa 250/25 mg. «Follow the instructions for use» was the most common response (13%). On the plus side, nearly half of the respondents (43%) were told about the potential adverse effects of levodopa and carbidopa by both the doctor and the chemist. Based on the findings, practical guidelines for the use of levodopa and carbidopa in the treatment of Parkinson's disease have been devised.

5) We developed practical recommendations for all participants of the

treatment process (pharmacists and pharmacy visitors / patients / caregivers) about specifics pharmacological care when using levodopa and carbidopa in the treatment of Parkinson's.

6) Considering all of the above, the improvement of issues related to the pharmaceutical care of patients taking levodopa/carbidopa drugs for the treatment of Parkinson's disease remains an urgent problem and requires further study and improvement.

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APPENDIX

Appendix A

КЛІНІЧНА ФАРМАЦІЯ В УКРАЇНІ ТА СВІТІ

2023

Міністерство охорони здоров'я України
Національний фармацевтичний університет
Кафедра клінічної фармакології
та клінічної фармації

The Ministry of HealthCare of Ukraine
National University of Pharmacy
Department of Clinical Pharmacology
and Clinical Pharmacy

СЕРТИФІКАТ
CERTIFICATE

№ 268

Цим засвідчується, що

This is to certify that

Mahmoud abou Warda

брав(ла) участь у роботі Всеукраїнської науково-практичної Internet-конференції з міжнародною участю "Клінічна фармація в Україні та світі", присвяченої 30-річчю заснування кафедри клінічної фармакології та клінічної фармації Національного фармацевтичного університету
16-17 березня 2023 р., м. Харків

participated in the All-Ukrainian scientific and practical Internet-conference with international participation "Clinical pharmacy in Ukraine and the World", dedicated to the 30th anniversary of the Department of Clinical Pharmacology and Clinical Pharmacy of the National University of Pharmacy founding
March 16-17, 2023, Kharkiv

В.о. ректора НФаУ, проф. Алла КОТВІЦЬКА

Проректор з науково-педагогічної роботи НФаУ, проф. Інна ВЛАДИМИРОВА

Завідувачка кафедри клінічної фармакології та клінічної фармації, проф. Катерина ЗУПАНЕЦЬ

Continuation of Appendix A

THE MINISTRY OF HEALTHCARE OF UKRAINE
NATIONAL UNIVERSITY OF PHARMACY
DEPARTMENT OF CLINICAL PHARMACOLOGY
AND CLINICAL PHARMACY

CLINICAL PHARMACY IN UKRAINE AND THE WORLD

MATERIALS
of the All-Ukrainian scientific and practical Internet-conference
with international participation, dedicated to the 30th anniversary
of the Department of Clinical Pharmacology and Clinical Pharmacy
of the National University of Pharmacy founding

March 16-17, 2023
Kharkiv

Registration certificate UkrISTEI
No. 543 dated December 19, 2022

Kharkiv
NUPh
2023

PROSPECTS FOR NEW DOSE FORMS OF COMPLEX DRUGS CONTAINING LEVODOPA AND CARBIDOPA

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Introduction. Parkinson's disease (PD) drugs can be divided into three categories. The generic (unbranded) name – co-careldopa is a combination of levodopa (LD) and carbidopa (CD). The brand name is Sinemet® is the name that the pharmaceutical company, MSD, uses to sell co-careldopa. It also may see that the medication is written as modified release (MR), controlled release (CR), and prolonged release medication (PR). All of these labels mean the same thing, but drug companies can choose which one to use with their drug. LD is the name used to describe one of the main types (classes) of drugs and is the «gold standard» for PD treatment. For some people with PD, protein (which is found mainly in meat, fish, eggs, cheese, beans, and pulses) seems to interfere with how well levodopa medications are absorbed by the body. Because of this, it may benefit from taking the medication 30-60 minutes before eating. It may also benefit from a protein redistribution diet, where patients take most of their daily protein in the evening. This can help the levodopa treatment to be more effective in the daytime when patients are likely to need it more. PD causes progressive disability that can be slowed but not halted by treatment. Therefore, the goal of medical management of PD is to control the signs and symptoms of the disease for as long as possible while minimizing adverse effects. The challenge in maintaining LD plasma levels within this progressively narrowing therapeutic window is complicated by LD's narrow absorption window, with absorption limited to the upper GI tract, as well as LD's short clearance half-life when taken with CD. As high levels of LD are associated with dyskinesia development, it is preferable to maintain peak LD levels just high enough for efficiency. Reducing LD dosage while maintaining stable LD levels

should help patients with PD maintain more consistent motor function.

Aim of the study. The search for new ways to deliver active ingredients to the intestines is one of the goals of improving the management of PD.

Materials and methods. To review the evidence base for LD-CD intestinal gel and Accordion Pill® using data from The National Center for Biotechnology Information (pubmed.ncbi.nlm.nih.gov). The following filters were included in the search: free full text, all article types (books and documents, clinical trial, meta-analysis, randomized controlled trial, review, and systematic review), and publication date of 5 years.

Results and discussion. LD-CD intestinal gel (LD-CD IG) – Duodopa – is a gel form of LD (co-careldopa) reserved for advanced and complex Parkinson's. It is pumped through a tube that is surgically inserted into the intestine. This means the dose of medication acts more quickly. LD-CD IG can help reduce involuntary movements as a side effect of medication, reduction in 'off'-time (motor fluctuations from drugs wearing off), and problems with symptoms at night. LD-CD IG is only suitable for a few people whose symptoms can't be controlled with more common drug treatments, such as levodopa tablets. Most frequent adverse events were related to the procedure or the device.

The Accordion Pill™ (AP) represents a novel gastric-retention oral delivery platform based on folded multilayer films (Intec Pharma, Jerusalem, Israel) to enhance pharmacokinetics (PK) and therapeutic benefit of challenging drugs. AP is characterized by one or more of the following: narrow absorption window (poor colonic absorption), narrow therapeutic window (maximum plasma concentrations correlate with adverse events and/or trough levels correlate with poor efficiency), poor solubility (low solubility, high permeability (Biopharmaceutics Classification System (BCS) class II) and low solubility, low permeability (BCS class IV) and act locally, in the stomach or in the upper part of the GI tract. Furthermore, AP allows multiple drug release profiles in a single capsule and can provide fixed-dose combinations. Phase II clinical trials have evaluated gastric retention and PK of AP in healthy volunteers and the efficacy and safety of AP-containing CD-LD (AP-CD-LD) in PD patients. AP was retained in the stomach for approximately 8 h, without special meal requirements. AP-CD-LD demonstrated improved absorption, more stable levodopa exposure, and improved time compared with immediate-release CD-LD in advanced PD patients. AP-CD-LD may achieve stable LD plasma concentrations with significantly fewer daily doses. Despite potential problems with intestinal motility, earlier clinical trials demonstrated that PD patients retained the AP for 11.8–13.9 h. AP-CD-LD consists of five layers with both immediate release and controlled release components for CD-LD fixed-dose combination. As high levels of LD are associated with the development of dyskinesia and deep troughs in LD availability are associated with pulsatile stimulation of dopamine receptors in the striatum, the results observed with AP-CD-LD are promising for providing efficiency while reducing risks of motor complications. AP-CD-LD is currently in Phase III clinical trials: a multi-center, global, randomized, double-blind, double-dummy, active-controlled, parallel-group study in adult subjects with fluctuating PD. – A Study to Assess the Safety and Efficacy of the Gastric-retentive AP-CD/LD in Advanced

Parkinson's Patients (Accordion Pill™, Sinemet®, Placebo-AP-CD-LD, and Placebo-Sinemet)

Conclusions. Continuous delivery of LD-CD IG offers a promising option for the control of advanced Parkinson's disease with motor complications. AP-CD-LD, with its controlled release and gastric retentive formulation, has demonstrated improved efficacy and safety in early clinical trials in patients with advanced PD, with a significant reduction in daily dosing. Pharmacists can help patients understand the medication they are prescribed and explain how to take it. If the patient has other illnesses or conditions and needs medication, the pharmacist can guide him/her on how to take these alongside Parkinson's medication. It is useful to keep the packaging for medication. This will help the patient to remember what the patient is taking. The patient can also record the name and strength of the medication and carry this list with him/her for when the patient needs it. This will be particularly useful in an emergency, as it will help medical professionals to understand what medication the patient takes.

Ф А 2.2.1–32-366

National University of Pharmacy

Faculty for foreign citizens' education
Department of clinical pharmacology and clinical pharmacy

Level of higher education master

Specialty 226 Pharmacy, industrial pharmacy
Educational program Pharmacy

APPROVED
Acting Head
of Department
of Clinical Pharmacology
and Clinical Pharmacy

_____
Tetiana SAKHAROVA
«02» of September 2022

ASSIGNMENT
FOR QUALIFICATION WORK
OF AN APPLICANT FOR HIGHER EDUCATION

Mahmoud Sami Arafa ABOUWARDA

1. Topic of qualification work: «Development of approaches to improving pharmaceutical care of Parkinson's disease patients»,
supervisor of qualification work: Tetiana ZHULAY, PhD, assistant.

approved by order of NUPh from «06th» of February 2023 № 35

2. Deadline for submission of qualification work by the applicant for higher education: April 2023.

3. Outgoing data for qualification work: Parkinson's disease, levodopa, carbidopa, effectiveness criteria, safety criteria, pharmaceutical care.

4. Contents of the settlement and explanatory note (list of questions that need to be developed):
to consider the epidemiology and medico-social significance of Parkinson's disease; to analyze recommendations for modern approaches to Parkinson's disease treatment; to create a questionnaire to conduct a survey for pharmacists about their awareness of intestinal gel containing levodopa and carbidopa use; to create a questionnaire to conduct a survey for pharmacy about their awareness of the rational use of levodopa-carbidopa oral drugs; to develop practical recommendations for pharmacists and pharmacy visitors / patients / caregivers on the specifics of pharmaceutical care when using levodopa and carbidopa in the treatment of Parkinson's disease..

5. List of graphic material (with an exact indication of the required drawings):
figures – 13

6. Consultants of chapters of qualification work

Chapters	Name, SURNAME, position of consultant	Signature, date	
		assignment was issued	assignment was received
1.	Tetiana ZHULAI, assistant of clinical pharmacology and clinical pharmacy department	02.09.2022	02.09.2022
2.	Tetiana ZHULAI, assistant of clinical pharmacology and clinical pharmacy department	02.09.2022	02.09.2022
3.	Tetiana ZHULAI, assistant of clinical pharmacology and clinical pharmacy department	02.09.2022	02.09.2022

7. Date of issue of the assignment: «02» September 2022

CALENDAR PLAN

№ з/п	Name of stages of qualification work	Deadline for the stages of qualification work	Notes
1.	Conducting a literature review on the issues of the work.	September-November 2022	**done**
2.	Conducting a survey of pharmacists and patients.	December 2022	**done**
3.	Experimental data processing.	January-February 2023	**done**
4.	Writing the qualification work.	March-April 2023	**done**
5.	Registration of the work and accompanying documents and submission to the Examination Committee of the NUPh.	April 2023	**done**

An applicant of higher education _____ Mahmoud Sami Arafa ABOUWARDA

Supervisor of qualification work _____ Tetiana ZHULAI

ВИТЯГ З НАКАЗУ № 35
По Національному фармацевтичному університету
від 06 лютого 2023 року

нижченаведеним студентам 5-го курсу 2022-2023 навчального року, навчання за освітнім ступенем «магістр», галузь знань 22 охорона здоров'я, спеціальності 226 – фармація, промислова фармація, освітня програма – фармація, денна форма здобуття освіти (термін навчання 4 роки 10 місяців та 3 роки 10 місяців), які навчаються за контрактом, затвердити теми кваліфікаційних робіт:

Прізвище студента	Тема кваліфікаційної роботи		Посада, прізвище та ініціали керівника	Рецензент кваліфікаційної роботи
• **кафедри клінічної фармакології та клінічної фармації**				
Абуварда Махмуд Самі Арафа	Development of approaches to improving pharmaceutical care of Parkinson's disease patients	Розробка підходів до удосконалення фармацевтичної опіки пацієнтів з хворобою Паркінсона	асистент Жулай Т.С.	професор Оклей Д. В.

Підстава: подання декана, згода ректора

Ректор

Вірно. Секретар

Ф А2.8-47-110

ВИСНОВОК

Комісії з академічної доброчесності про проведену експертизу

щодо академічного плагіату у кваліфікаційній роботі

здобувача вищої освіти

№ 114246 від « 29 » травня 2023 р.

Проаналізувавши випускну кваліфікаційну роботу за магістерським рівнем здобувача вищої освіти денної форми навчання Абуварда Махмуд Самі Арафа, 5 курсу, _____ групи, спеціальності 226 Фармація, промислова фармація, на тему: «Розробка підходів до удосконалення фармацевтичної опіки пацієнтів з хворобою Паркінсона / Development of approaches to improving pharmaceutical care of Parkinson's disease patients», Комісія з академічної доброчесності дійшла висновку, що робота, представлена до Екзаменаційної комісії для захисту, виконана самостійно і не містить елементів академічного плагіату (компіляції).

Голова комісії,
професор **Інна ВЛАДИМИРОВА**

2%

28%

Ф А 2.2.1-32-356

REVIEW

of scientific supervisor for the qualification work of the master's level of higher education of the specialty 226 Pharmacy, industrial pharmacy

Mahmoud Sami Arafa ABOUWARDA

on the topic: «Development of approaches to improving pharmaceutical care of Parkinson's disease patients»

Relevance of the topic. The theme of the qualification work chosen by the higher education applicant is relevant, because today, in connection with the aging of the global population, Parkinson's disease has almost the highest rates of spread among neurological diseases. According to statistics from the WHO, the incidence of PD is estimated at 4.5–16/100,000 people/year. Therefore, the improvement of approaches to pharmaceutical care for patients with Parkinson's disease for all participants in the treatment process, based on knowledge of the clinical pharmacology of Parkinson's drugs, is of particular relevance.

The practical value of conclusions, recommendations, and their validity. The research conducted in this qualification work is the basis for further clinical and pharmaceutical research, development, and implementation of principles for optimizing the rational use of levodopa and carbidopa for the long-term treatment of Parkinson's disease. The implementation of these principles and provisions into practical medicine and pharmacy will increase the effectiveness and safety of Parkinson's disease treatment.

Assessment of work. The work is performed at a sufficient scientific and methodological level. In terms of relevance, scientific novelty, and practical significance, it fully meets the requirements for qualification works.

General conclusion and recommendations on admission to defend. The work is performed in full, designed in accordance with the current requirements for the qualification works at the National University of Pharmacy, and can be recommended for submission to the EC for further defense.

Scientific supervisor _____ Tetiana ZHULAI

«11» April 2023

Ф А 2.2.1-32-356

REVIEW

for qualification work of the master's level of higher education, specialty 226 Pharmacy, industrial pharmacy

Mahmoud Sami Arafa ABOUWARDA

on the topic: «Development of approaches to improving pharmaceutical care of Parkinson's disease patients»

Relevance of the topic. The qualification work submitted for review is quite relevant, given the high incidence of Parkinson's disease and its increasing trends. According to experts' estimates, there are 6.9 million sufferers in the world, and in 2040 their number will increase to 14.2 million, as humanity is rapidly aging. Although Parkinson's disease is incurable, many drugs and treatments are available to control the condition and symptoms. Drug treatment is usually the mainstay of treatment for Parkinson's disease, but the patient must also have access to specialists from different health and social services teams who can offer different types of therapy.

The theoretical level of work. The literature review conducted theme of the study illustrates the lack of patients' adherence to Parkinson's disease long-term treatment with levodopa-carbidopa drugs to date and outlines the prospects for research.

Author's suggestions on the research topic. The provisions of the author of the work on medication adherence are of practical importance for the modern healthcare system.

The practical value of conclusions, recommendations, and their validity. Based on the research results, approaches to the rational use of Parkinson's drugs have been developed using the example of levodopa-carbidopa. The author discusses the main approaches to increasing patients' adherence to long-term treatment of Parkinson's disease. Practical recommendations for all healthcare providers are proposed.

Disadvantages of work. Single grammatical and spelling errors do not affect the overall positive assessment of the work.

General conclusion and assessment of the work. The work meets the requirements for qualification work in NUPh and can be recommended for defense.

Reviewer _____ ass. prof. Denys OKLEI

«15» April 2023

МОЗ України
Національний фармацевтичний університет

ВИТЯГ З ПРОТОКОЛУ №10

Засідання кафедри клінічної фармакології та клінічної фармації

м. Харків «19» квітня 2023 р.

СЛУХАЛИ: Про представлення до захисту в Екзаменаційній комісії випускної кваліфікаційної роботи на тему: **«Розробка підходів до удосконалення фармацевтичної опіки пацієнтів з хворобою Паркінсона» / «Development of approaches to improving pharmaceutical care of Parkinson's disease patients»**
здобувача вищої освіти 5 курсу, спеціальність – 226 Фармація, промислова фармація, освітня програма – Фармація, ступінь вищої освіти – магістр, термін навчання – 4 р. 10 міс., денна форма навчання, НФаУ 2023 року випуску

Махмуд Самі Арафа Абуварда
прізвище, ім'я та по батькові

Керівник: асистент кафедри клінічної фармакології та клінічної фармації, к.мед.н. Жулай Т.С.

Рецензент: професор закладу вищої освіти кафедри хірургічних хвороб Харківського національного університету імені В. Н. Каразіна, д.мед.н., доцент Оклей Д.В.

В обговоренні кваліфікаційної роботи брали участь:
В.о. зав. кафедри, професор Т.С. Сахарова; професор В.А. Мороз; професор С.К. Шебеко; доцент О.О. Андрєєва; доцент Н.П. Безугла; доцент В.В. Пропіснова; доцент С.В. Місюрьова; доцент І.А. Отрішко; доцент О.О. Тарасенко; доцент К.М. Ткаченко; асистент С.М. Зімін; асистент Т.С. Жулай; асистент Н.В. Давішня; асистент Т.Ю. Колодєзна; асистент К.В. Вєтрова; асистент Ю.В. Тимченко

ПОСТАНОВИЛИ: Рекомендувати до захисту в ЕК кваліфікаційну роботу здобувача вищої освіти

Махмуд Самі Арафа Абуварда
прізвище, ім'я та по батькові

На тему: **«Розробка підходів до удосконалення фармацевтичної опіки пацієнтів з хворобою Паркінсона» / «Development of approaches to improving pharmaceutical care of Parkinson's disease patients»**

В.о. завідувачки кафедри _____ Тетяна САХАРОВА
(підпис)

Секретар _____ Катерина ТКАЧЕНКО
(підпис)

Ф А2.2.1-32-042

НАЦІОНАЛЬНИЙ ФАРМАЦЕВТИЧНИЙ УНІВЕРСИТЕТ

ПОДАННЯ
ГОЛОВІ ЕКЗАМЕНАЦІЙНОЇ КОМІСІЇ
ЩОДО ЗАХИСТУ КВАЛІФІКАЦІЙНОЇ РОБОТИ

Направляється здобувач вищої освіти Махмуд Самі Арафа АБУВАРДА до захисту кваліфікаційної роботи

за галуззю знань 22 Охорона здоров'я
спеціальністю 226 Фармація, промислова фармація
освітньою програмою Фармація
на тему: «Розробка підходів до удосконалення фармацевтичної опіки пацієнтів з хворобою Паркінсона» / «Development of approaches to improving pharmaceutical care of Parkinson's disease patients»

.

Кваліфікаційна робота і рецензія додаються.

Декан факультету _____ / Світлана КАЛАЙЧЕВА /

Висновок керівника кваліфікаційної роботи

Здобувач вищої освіти Махмуд Махмуд Самі Арафа Абуварда виконав весь необхідний обсяг робіт. Кваліфікаційна робота може бути рекомендована до подачі в ЕК НФаУ для подальшого її захисту.

Керівник кваліфікаційної роботи

_____ Тетяна ЖУЛАЙ

«11» квітня 2023 року

Висновок кафедри про кваліфікаційну роботу

Кваліфікаційну роботу розглянуто. Здобувач вищої освіти Махмуд Самі Арафа АБУВАРДА допускається до захисту даної кваліфікаційної роботи в Екзаменаційній комісії.

В.о. завідувачки кафедри
клінічної фармакології та клінічної фармації

_____ Тетяна САХАРОВА

«19» квітня 2023 року

Qualification work was defended
of Examination Commission on
«___» June 2023
with the grade _____

Head of the State Examination Commission,
DPharmSc, Professor
_____ / Oleh SHPYCHAK /