


## CHAPTER 12

# Relationship between pharmacology and Florence Nightingale's theory

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### Yoel López Gamboa

<https://orcid.org/0000-0002-9596-443X>  
City of Guayaquil. Guayas Province. Ecuador  
E-mail: [yoel111975@gmail.com](mailto:yoel111975@gmail.com)

### Yoeldis Gamboa Pellicier

City of Guayaquil. Guayas Province. Ecuador  
E-mail: [gamboa41@gmail.com](mailto:gamboa41@gmail.com)

### Yanet Rodríguez Cantillo

<https://orcid.org/0000-0001-5028-9576>  
City of Guayaquil. Guayas Province. Ecuador  
E-mail: [alfrelia@gmail.com](mailto:alfrelia@gmail.com)

### ABSTRACT

In the mid-nineteenth century, nursing as a profession was founded by Florence Nightingale, although it was not until the second half of the twentieth century that significant advances were truly made in the development of the profession. With the aim of establishing the relationship that exists between Florence Nightingale's theory and Pharmacology, the

present work was carried out. A bibliographic review of the current state of the subject was made in the Google academic, SciELO, Dialnet, and PubMed databases, with the keywords: Chronobiology, Chronopharmacology, Biological rhythms and Chronopharmacokinetics. In this review, it was evidenced that there is a direct association between the time of day in which the drugs are administered, and the pharmacological effects, especially due to changes in their pharmacokinetic variability, factors that also influence their safety, and in pharmacodynamics. The physiological processes that occur in our body follow the course of biological rhythms, so they must be taken into consideration in pharmacotherapy in order to guarantee greater therapeutic efficacy and greater safety. The elements described allow us to affirm the relationship between nature and man, as postulated by Nightingale, and pharmacology.

**Keywords:** Chronobiology, Chronopharmacology, Biological rhythms, Chronopharmacokinetics.

## 1 INTRODUCTION

In the mid-nineteenth century nursing was founded as a profession by Florence Nightingale, although it was not until the second half of the twentieth century that truly significant advances were made in the development of the profession, and the acquisition of skills by nursing staff, thanks to the theoretical and practical advances that were achieved at that time. The millenary practice of care from this period began to find theoretical justification through observation, description, explanation, prediction and control of the phenomena of their field of action, especially the care of individuals, family and community. (Naranjo-Hernández et al., 2020).

Theory coupled with practice has managed to base the actions of nursing as a science, which previously was only limited to the fulfillment of medical orders. This profession is not only dedicated to the exercise of the practical activity of health care, but also to education and research associated with the solution of problems arising from the exercise of the profession as such. The theory has contributed to the nursing the analyses and logical reasonings and the clarification of its ethical acting before in the studied phenomena. (Baeza et al., 2018).

According to Florence, every woman at some point had to serve as a nurse to take care of someone's health. She defined the nurse's responsibility to care for the health of others in her nursing note, where she also defined the guidelines for nursing practice and gave advice that would allow women to think like nurses when caring for the health of individuals. (Naranjo-Hernandez et al., 2020).

Florence Nightingale's theory fundamentally emphasizes the environmental determinants in the health-disease process, which has been a source of astonishment because it constituted a very revolutionary thought for her time where there were other theories generally enunciated by physicians, with emphasis on the biological. In this scenario Florence, defined the essence of the nursing profession that made it distinctive, and consisted of putting the patient in the best conditions for nature to act on him, also defining that nursing as a profession was based on the knowledge of people and their environment, which was a different vision seen until then by doctors for their practice of the profession. (Cano & Carmen, 2004)

Nightingale's postulates revolve around three key elements: the relationship of the patient with his environment, the relationship of the nurse with the patient and the relationship of the nurse with the patient's environment. (Cano & Carmen, 2004) Within these three elements, according to experts the least explained by Florence is the dimension of the relationship between the nurse and the patient, however, she made several observations in this regard. (Martínez Bentancourth, 2018)

In this order he postulated and I quote: "The nurse should explore the preferences of patients about the schedules of treatments and care, and about the contents and forms of food, whenever possible". (Cano & Carmen, 2004)

In relation to this last affirmation and putting into context the influence that the times of day in which drugs are administered can have on their effectiveness and safety, this paper aims to approach a branch of pharmacology that studies this phenomenon; Chronopharmacology.

## 2 METHODS

A bibliographic review of the current state of the subject was carried out in the databases Google Scholar, SciELO, Dialnet, and PubMed, with the keywords: Chronobiology, Chronopharmacology, Biological Rhythms, Chronopharmokinetics, looking for some level of association between Florence Nightingale's theory and Pharmacology. The review was carried out in English and Spanish. We used bibliography preferably from the last 5 years. However, previous publications with relevant elements that could argue the following work were taken into account. Thirty-eight articles with related topics were found, of which 15 were taken into consideration because they dealt with the topic in question in a more comprehensive manner.

### 3 RESULTS AND DISCUSSION

There is a direct association between the time of day in which the drugs are administered, and the pharmacological effects, especially by modifications in the pharmacokinetic variability of the drugs, factors that also influence in the safety of these, and in the pharmacodynamics. Biological rhythms affect among other factors the metabolism and elimination of drugs; in metabolism mainly because the liver enzymes with metabolic functions are sensitive to circadian oscillations, which directly influences the pharmacological effects and also the toxic effects. (Molina Cabrera, 2015), (Zhao et al., 2020).

The different scientific studies carried out in the field of chronobiology have eloquently demonstrated the influence that different biological rhythms have on the vital functions of living organisms. The biological rhythms are related to certain hormonal release at different times of the day that condition the behavior of human physiology, which in turn influences the organism at certain times of the day to present a better assimilation of pharmacological treatments. (Molina-Rodríguez & Akle-Álvarez, 2016).

Chronopharmacology is a relatively new area of study, which has modified the way to visualize some postulates that had been taken for granted regarding the effectiveness of pharmacological therapies, its basis lies in the concepts of chronobiology, which study the influence of biological rhythms in the interactions that exist at the cellular and tissue level with the environment. (Castellanos et al., 2016)

Although the concepts of chronobiology and chronopharmacology are not very new, their importance has not been understood by medical personnel and other health actors, which is why they are not generally taken into account when indicating a pharmacological therapy, nor have they been properly integrated into the behavior of the health-disease process, so biological rhythms are not taken into account and the biology of human beings is broken into without considering the consequences for health, or for the effectiveness of pharmacotherapy.(Camprubí Andaluz, 2017).

The biological and equilibrium processes that occur in the human organism course in time in a cyclical manner, gradually passing through several states until reaching their maximum and minimum values, within which we can mention the following: female menstrual cycle, cell cycle, sleep-wake cycle, hormonal variations of cortisol, melatonin, adrenaline, serotonin, among others. These variations determine that the organism is apt for certain functions in the schedules where the concentrations of these hormones present the highest levels of fluctuations. (Escagedo Cagigas, 2019)

In line with what was explained above, below are some health damages that can be caused by a break in the balance of some of the biological rhythms that occur in our body. Considering that ultradian or high frequency rhythms are those that occur in time less than 20 hours, infradian or low frequency rhythms are those that occur in time greater than 28 hours, and circadian rhythms are those that occur between 20 and 28 hours.(Tamosiunas & Toledo, 2010)

Table 1. Relationship between some biological cycles, the fisiology and pathological response of the organism.

No	Biological rhythms	Physiology	Pathology
1	Circadians	Sleep-wake cycle. Body temperature with afternoon acrophase. Morning acrophase (maximum peak): catecholamines, cortisol, platelet aggregability.	Sleep disorders, jetlag syndrome. Alterations due to rotating shift work. Higher incidences of acute myocardial infarction and ischemic-hemorrhagic stroke with a higher incidence in the mornings.
2		Renin-angiotensin-aldosterone system, blood viscosity, platelet activity, and blood pressure, Acrophase (nocturnal peak). Secretion of hydrochloric acid, hormone growth hormone, melatonin and bronchial reactivity	Increased incidence of gas troduodenal ulcers at night. Increased incidence of bronchospasm crises at night. Acute pulmonary edema.
3	Ultradians	Heart rate, respiratory rate and hormone secretion pulsating	Cardiac arrhythmias, polypnea, bradypnea
4	Infradians	Menstrual Cycle	Premenstrual Dysphoric Syndrome

**Source:** Adapted from the scientific article. Chronopharmacology: a new aspect to consider in the variability of therapeutic response.

The variability of the therapeutic response of drugs depends on different factors, and in each individual is usually expressed in a different way, they are very complex mechanisms and of different nature, ranging from the fisicochemical properties of drugs, through the pharmacotenic used in the development, to age differences, sexual, genetic, polymedication, habits of drug consumption and prescription, as well as influyen also the fisiopathological situation of each individual. (Castellanos et al., 2016)

(Tamosiunas & Toledo, 2010) states that the aforementioned aspects are causes of modifications of the pharmacokinetic and pharmacodynamic variability of drugs, which coincides with what was stated by the authors Castellanos and Escobar. In addition, they state that the endogenous response of the organism to the different biological rhythms, in terms of biochemical, physiological, hormonal and pathological responses, also modifies the pharmacokinetic and pharmacodynamic parameters of drugs and therefore modifies the pharmacological response after the consumption of certain drugs, an approach in which the authors cited above also agree.

According to afirma (Tamosiunas & Toledo, 2010).According to the study of chronopharmacokinetics, chronopharmacokinetic studies are responsible for evaluating the temporal variation of different pharmacokinetic parameters, among which the half-life time and the time in which the maximum concentration of the drug is reached in the organism stand out; the rhythmic variation of several biological processes such as gastrointestinal secretion, blood flow, hepatic flow, glomerular filtration, affect the absorption, distribution, metabolization and elimination of drugs, so it cannot be guaranteed that these pharmacokinetic parameters are the same at different times of the day.

What has been stated by the previous authors is corroborated by the pharmacokinetic studies carried out to explain the factors that modificate the pharmacological effects of drugs, whether they are those that depend on the drugs through their fisicochemical and technological properties, as well as those that depend on the patient. (Molina Cabrera, 2015), (Bicker et al., 2020).

There are studies that have shown circadian variations at the hepatic level in cytochromes p450A3 and N-acetyltransferase which act in the metabolism of drugs in both phase I and phase II, this finding may increase or decrease the effect of the first hepatic step depending on the time of day in which the drugs are administered, which presupposes a variation in the pharmacological effects of the same. (Tamosiunas & Toledo, 2010). It is worth noting that chronopharmacokinetics is of vital importance for those drugs that have a narrow therapeutic margin such as: theophylline, lithium, carbamazepine, valproic acid, and digoxin, among others. (Molina Cabrera, 2015)

There is evidence of several drugs that when given in the same concentrations and in similar environmental conditions, where only the time of day has been modified, show different plasma concentrations. For example, in a study conducted by Orlando et al. in Uruguay, they found different concentrations of digoxin when given under the conditions explained above, only varying in that it was given in the morning in one case and in the other at night, and it was found that the maximum concentration of the drug was higher at night than in the morning.(Tamosiunas & Toledo, 2010),(Alloway et al., 2020)

The previous finding could be explained by the results obtained in other investigations where it is explained that in general in the mornings the metabolic processes are accelerated (Atienza Sánchez et al., 2016). A similar explanation could be given to the fact that other research has shown that thefilin when administered in the evening has better safety and efficacy than when administered at other times of the day. (Tamosiunas & Toledo, 2010).

Taking into consideration the information provided by chronopharmacology, therapeutic guidelines have been established for different pathologies, among which we can mention: treatment for hypercholesterolemia, because it is known that at night, between midnight and early morning endogenous synthesis of cholesterol increases, it is supplied lipid-lowering drugs in the late afternoon in order to reach maximum concentrations at times of increased synthesis. Arterial hypertension usually increases between six o'clock in the morning and up to twelve o'clock in the day, so it is recommended to administer the medication during the previous night in order to guarantee maximum concentration in the morning hours; in osteoarthritis the symptoms are more intense in the afternoon, so medication should be administered in the mornings. (Molina Cabrera, 2015), (Alloway et al., 2020)

Glucocorticoids are a group of drugs that are very frequently used in the current therapeutic arsenal, especially in inflammatory diseases and diseases of the immune system, among which bronchial asthma, rheumatoid arthritis, Crohn's disease, among others, stand out; It is known that the biological rhythms that affect our body influence the release of endogenous cortisol in our body, which is the first glucocorticoid in humans and if this element is not taken into account when administering these drugs can be affected by

the regulation of cortisol by the hypothalamus and inhibit the physiological production of this substance. (Scherholz et al., 2019)

There are many pharmacological strategies that take into consideration the variations of circadian rhythms, precisely taking into consideration the affectations that they cause in the different hormones of our human organism at different times of the day. The endocrine dysregulation produced by the release of cortisol can lead to the development of cancerous and metabolic diseases, depression, insomnia, among others; in these cases applying therapeutic mechanisms based on chronopharmacology is vital to achieve more accurate therapeutic effects that can influence biological, behavioral, biochemical and physiological changes. (Ohdo et al., 2019), (Bicker et al., 2020)

#### 4 CONCLUSIONS

- ✓ The physiological processes that occur in our body follow the course of biological rhythms, so they must be taken into consideration in pharmacotherapy in order to ensure greater therapeutic efficacy and greater safety, which evidences the relationship between man and nature according to the theory of Florence Nightingale and pharmacology.
- ✓ Chronopharmacology plays an important role in the pharmaceutical industry, because it allows to adjust the design of pharmaceutical forms to the characteristics of the different biological rhythms, thus favoring the pharmacological effects of drugs.
- ✓ Adequate knowledge of biological rhythms allows modification of the pathophysiological course of many diseases and thus a better quality of life for patients.



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