

A LITERATURE REVIEW ON “BIOLOGICAL CLOCK: BIOLOGICAL RHYTHMS AND HUMAN CIRCADIAN RHYTHMS”**Mohammed Zeeshan Danish*¹ and Dr. Muhammed Saleem²**¹Student, Deccan School of Pharmacy,²Professor, Deccan School of Pharmacy,

Department of Pharmaceutical Biotechnology, Deccan School of Pharmacy, Dar-us-salam,
Aghapura, Hyderabad 500001, Telangana, India.

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Corresponding Author*Mohammed Zeeshan
Danish**

Student, Deccan School of
Pharmacy, Department of
Pharmaceutical
Biotechnology, Deccan
School of Pharmacy, Dar-
us-salam, Aghapura,
Hyderabad 500001,
Telangana, India.

ABSTRACT

Every living organism in this world has a Complex system of cells which has own pace of functioning as well as maintaining the human health. Cells in our body are individually responsible for every condition that occurs during normal physiology or in disease conditions. Every cell has its own rhythms which are called biological rhythm patterns which vary from cell to cell. In this article we will have a detailed description about how a biological clock works in our body & how circadian rhythms change the body physiology and health of an individual. The article also discusses about the timely facts of the biological clock working in our body non-stop. Any disruption or interruption in the rhythms may lead to many disorders like cardiac problems, sleep disorders which are mentioned in the article. Such changes in the rhythms may also affect the hormonal levels or hormonal regulations in the body which may lead to other diseases. There are many ways to manage or treat such disorders which occur

due to disturbance in the biological rhythms mainly circadian rhythms in human body. Resetting the biological clock or the sleep clock and improvement can be done by natural methods i.e. home remedies and lifestyle changes. As we all know occurrence of good sleep gets human body to improve resting which improves health indirectly. The only motive behind this article is to make this world understand that health is a priceless wealth now days.

KEYWORDS: Biological clock, Circadian Rhythms, Sleep Disorders and Natural Remedies.

INTRODUCTION

Biological rhythms represent basic property of most living organisms ranging from varieties of bacteria and single-cell organisms to multi cellular plants and animals. Our body includes of a full system of biological clocks that coordinate superbly with one another and conjointly with the central clock that continues to be entrained with the external surroundings so we tend to sleep in harmony with our environment. In this article, we provide an overview of the biological rhythms seen in organisms followed by an outline of the human circadian rhythms. The importance of the circadian system in metabolism effecting our metabolic health and behavior has conjointly been mentioned. This review conjointly covers how the disruption of these circadian rhythms might cause many diseases in our body and includes some relevant measures for treatment.

The biological rhythms may be classified into differing types on the basis of period of each cycle:

(a) circadian rhythm: A rhythm of roughly on a daily basis (~24 hours) like sleep-wake cycle.

(b) Infradian rhythm: A rhythm of more than the period of circadian rhythm i.e. with a frequency less than one cycle in twenty eight hours, e.g. the 0.5 weekly Cycle (circasemiseptan) of human death, estrouscycle.

(c) Ultradian rhythm: A rhythm with a period of less than circadian rhythm (less than twenty hours)

(d) Circaseptan rhythm: A rhythm with a period of a week. Some secretion rhythms follow a roughly weekly cycle, as do patterns of kidney Transplant rejection.

(e) Circatrigintan or Circamensual rhythm: A rhythm with a period of about month, e.g. human cycle.

(f) Circannual rhythm: A rhythm with a period of a year (~365.25Days). Seasonal and reproductive rhythms in some animals follow a Circannual cycle. E.g. over-winter hibernation.

(g) Diurnal rhythm: This rhythm is extension of circadian however the people should be synchronizing with the day and night cycle wherever they awake and performance normally throughout daylight and sleep throughout Night hour.^[4, 7, 8, 9]

Four Timely Facts regarding Our Biological Clocks

- 1. They're Incredible Intricate:** Biological clocks consist of genes and proteins that operate in a feedback loop. Clock genes have particular instructions for creating clock proteins, whose levels increase and decrease during a regular cyclic pattern. This pattern successively regulates the activity of the genes.
- 2. Each organism has them—from alga to zebras:** several clock genes and proteins are similar across species, permitting researchers to form vital findings regarding human circadian processes by learning the clock elements of organisms like fruit flies, bread mould and plants.
- 3. Whether or not we're awake or asleep, our clocks keep ticking:** whereas they could get temporarily thrown off by changes in light-weight or temperature, our clocks sometimes will reset themselves.
- 4. Nearly everything regarding however our body works is tied to biological clocks:** Our clocks influence alertness, hunger, metabolism, fertility, mood and alternative physiological conditions. For this reason, clock dysfunction is related to varied disorders, which includes insomnia, depression, and diabetes. Even drug efficacious has been coupled to our clocks: Studies have shown that some medicine can be more practical if given earlier within the day.^[11]

NORMAL PHYSIOLOGY OF BIOLOGICAL CLOCK

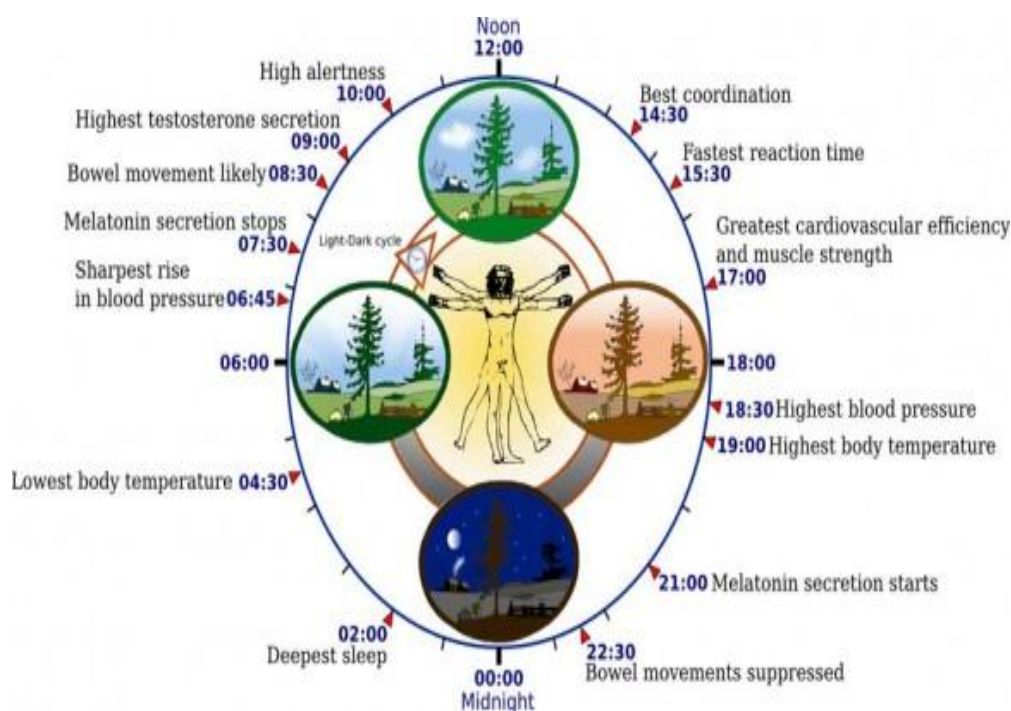


Fig. 1: Human circadian rhythms.^[12]

CIRCADIAN RHYTHMS

Circadian rhythms are generally physical, mental, and behavioral changes that occur daily and follow daily cycle. They respond primarily to light and darkness in an organism's setting. Sleeping in the dead of night and being awake throughout the day is an example of a light-related biological rhythms area unit found in most living things, together with animals, plants, and plenty of small microbes. The study of circadian rhythms is termed chronobiology. The intrinsic amount of the biological time in humans is about twenty five hours; however this is often sometimes changed by external cues like daylight.^[21,37] Research into the genetic and familial aspects of sleep disturbance, into sleep disorders in depression and different medical specialty conditions and into the connection of sleep disturbance in depression and neuroendocrine changes.^[36,37] Though diurnality of mood sometimes manifests itself by the subject feeling worse within the early morning, typically this is often reversed. Writer describes this for his own severe depressive illness: 'there was now something that resembled bifurcation of mood: lucidity of sorts within the early hours of the day, gathering murk within the afternoon and evening'.^[32] Thinking in reference to circadian rhythms in mood disorders was given more impetus owing to the invention of clock genes and cellular clocks, albeit there's no consistent finding that disruption of those clocks exist in mood disorders.^[24] it could be that clock gene expression outside the suprachiasmatic nucleus is concerned in mood regulation. This is often a matter for future research. It has been suggested that there could also be a shortened rhythm, of less than twenty four hours, in patients with semi-permanent psychosis. Abnormalities of circadian rhythms have conjointly been represented, however not totally supported, in anorexia and in individuals with abnormal personalities.^[25]

Circadian Rhythm Sleep Disorders

These are quite common disorders caused by misalignment between the sleep amount and the physical or social 24-h environmental cycle. The blind people and night-shift/rotating shift employees are a lot likely to develop these sleep disorders.

There is a relationship between disturbance in sleep and psychiatric disorder; psychological state might cause result in sleep disturbance, disturbed sleep might precipitate psychiatric symptoms or the two might occur together but independently. The International Classification of Sleep Disorders subsumes eighty five sleep disorders into nine classes including.^[2]

The circadian sleep disorders (CRSD) include: —

- Delayed sleep phase Syndrome

- Advanced sleep phase syndrome
- Non 24hr sleep-wake syndrome
- Irregular sleep-wake rhythm disorder
- circadian desynchrony
- Shift work sleep disorder
- Jet lag disorder
- Premenstrual syndrome
- Insomnias

Delayed sleep phase Syndrome A circadian sleep disorder within which the individual's internal body clock is delayed with relevance external day/night cycle, Falls asleep late in night, generally between 1:00am and 6:00am and awakens within the late morning or within the afternoon. Functional impairment is seen in daytime if total sleep time is reduced and designation by stable sleep delay in a minimum of 1 week of sleep log at the side of delay in CBTM & DLMO with exclusion of different causes, Prevalence of 5-10% and a lot of common in adolescents & young adults.

Advanced sleep phase syndrome Advanced sleep phase syndrome (ASPS) could be a pathological extreme of the morning lark phenotype. They usually fall asleep (doze off) at around 7:30 PM and spontaneously awaken at around 4:30 AM. Functional impairment happens within the late afternoon & evening when sleepiness begins and diagnosis includes confirmation of advanced temporal arrangement of sleep period with a sleep log for 7 days with exclusion of alternative causes, Prevalence is nearly 1% in middle aged people, seems additional common with advancing age.

Non 24hr sleep-wake syndrome Circadian rhythm that free runs at a period of its endogenous circadian clock even within the presence of your time cues. So, sleep wake period gradually shifts to later in day as time advances and diagnosis of increasingly delayed sleep-wake times with a period of more than 24hrs for 7 days in sleep log. Most common in blind due to failure of light signals to transmit to SCN. In sighted, secondary to diminished sensitivity to light as entraining agent or exceedingly long intrinsic circadian rhythm.

Irregular sleep-wake rhythm disorder Lack of clearly distinct sleep-wake cycles leading to symptoms of insomnia or sleepiness. Night time sleep is truncated and shows poor consolidation, daytime has frequent, irregular naps. Sleep logs show a minimum of 3

irregular sleep bouts throughout 24-hr period over every week. Mostly seen in institutionalized patients with dementia & in youngsters.

Circadian Desynchrony This happens in Travel across multiple time zones (jet-lag) and shift work is that the most typical causes of circadian desynchrony. Epidemiological studies have shown that ladies operating night shifts have a considerably elevated risk of breast carcinoma.

Shift work sleep disorder Artificial lighting has allowable the manufacturing and service industries to work round the clock. As a result, shift employees are perpetually experiencing the effects of circadian desynchrony as they struggle to entrain to an ever changing light–dark cycle. Diagnostic criteria include sleep disorder or excessive sleepiness, temporal relationship with work, present for a minimum of 1 month, 7-daysleep log.

Jet lag disorder Jet lag is that the condition of one's circadian clock being desynchronized from the local time ensuing from fast long distance Trans meridian (east–west or west–east) travel, as on an airplane. The condition of jet lag might last many days, and a recovery rate of 1 day per time zone crossed could be a fair guideline. Air traveler who fly west usually complain of issue maintaining sleep & early morning awakenings whereas those flying east have issue with initiating sleep.

Premenstrual syndrome Recurrence of symptoms in the premenstrual 5-10 days (luteal phase) with absence in the postmenstrual (follicular phase) is seen in 30-80% of reproductive women. Psychological symptoms: disabling tension, severe & sudden mood swings, suicidal depression and lethargy. Physical symptoms: It includes headache, acne energy loss. It is the timing instead of the character of symptoms that indicates the diagnosis. To ascertain a pattern, keep a prospective record of her symptoms on a calendar for a minimum of 2 menstrual cycles. PMS has inflated risk for depression.^[19, 31]

INSOMNIA Insomnia implies subjective dissatisfaction with the period or quality of sleep^[27] Formally, insomnias are outlined by issue with sleep initiation and/or maintenance, and final awakenings that occur prior to the established wake-up time.^[18] The individual might complain that the period of sleep is simply too short; or that sleep feels broken, less refreshing or insufficiently deep; sleep disorder is relatively common in girls and in older individuals.^[1, 23]

SIX Hormones That Can Affect Your Sleep

Our hormones are answerable for variety of changes that occurs in our body – they assist us to grow, to breed, they regulate our appetite and that they also manage our sleep. It's hardly stunning then that completely different hormones will have an effect on our sleep patterns in several ways.

1. Oestrogen

Oestrogen may be found in both men and women. It's usually related to reproductive health, taking major and crucial part in menstrual cycle; but, oestrogen also performs a range of completely different functions.

When do issues occur? As you progress through life, your levels of oestrogen will fluctuate, significantly during menstrual cycle if you're women. However, as you approach menopause, your levels of this hormone will plummet that brings a range of tell-tale symptoms, like irregular periods, hot flushes, mood swings and muscle and joint pain.^[14]

2. Progesterone

Progesterone is best called a female sex hormone – its name is virtually derived from 'promoting gestation.' It helps to sustain the liner of your uterus just in case of pregnancy, that is why women experiences high progestogen levels when ovulating, before they eventually decline. Progestogen is additionally important for healthy brain performance generally being classed as a neurosteroid. It has natural anti-anxiety.

When do issues occur? When progestogen levels begin to fall, either due to menstruation or menopause, it will cause problems with your sleep. If you suffer from low progestogen levels throughout menses, it will sometimes hint that your levels of oestrogen are much higher, during which you'll begin to experience symptoms like mood swings, fluid retention and cramping.^[14]

3. Testosterone

It is also known as male sex hormone. Testosterone isn't simply exclusive to men it also plays a vital role in feminine health too. In each sex, testosterone works to support reproductive health and in men, it conjointly helps to control muscle and bone mass too.^[17]

When do issues occur? Men don't usually experience a steep fall in testosterone. Instead, it step by step declines over a period of years. Low levels of testosterone will be related to sleep

issues. For example, testosterone levels usually fluctuate throughout the day and it's been shown that levels are at their highest throughout rapid eye movement sleep.^[13]

5 – Cortisol and Melatonin

These 2 hormones on this list have a lot of direct impact on your sleep cycle, and that they are thus interlinked that it's not possible to say one without another. Cortisol and Melatonin are the 2 main hormones that regulate your sleep pattern. Cortisol is usually called a 'stress hormone' and it's made by adrenal glands. It helps to control your metabolism and reduces inflammation and, once it's discharged, it raises your glucose levels and blood pressure level. As a part of circadian rhythm, in early hours of morning the levels of cortisol are elevated which helps which helps you feel refreshed and as the day progresses, your levels of cortisol can step by step decline as a lot of melatonin is discharged within the hours before you go to bed. Melatonin, or the sleep hormone, is produced by pineal gland and works with cortisol. Once your optic nerves discover natural light decreasing, they're going to send a message to your neural structure, which is able to trigger the discharge of melatonin to assist you relax and feel drowsy in preparation for sleep. Usually when cortisol levels increases the melatonin decreases and vice versa.

What happens once this balance is interrupted? Finally, few devices will suppress your production of melatonin. Melatonin is sometimes made as a response to an absence of natural light. Night-time encourages you to sleep however, if your optic nerves discover light waves that are just like ultraviolet light, it will trick your hypothalamus into believing that it's still daylight outside, and thus you ought to be awake. Sadly, most computers, televisions, tablets and sensible phones emit a blue lightweight wave that has this specific effect thus, binging on Netflix or trawling through social media on your sensible phone before bed will result in insomnia!

6 – Thyroid

Your Thyroid gland is located just under the larynx and produces 2 hormones, triiodothyronine and thyroxin. These 2 hormones facilitate to control your metabolic rate, digestive function and brain development thus, within the grand theme of things; they're each pretty vital, particularly when it comes to your mood.

When do issues occur? Problems tend to occur with your thyroid once your thyroid gland is either too active (hyperthyroidism) or not active enough (hypothyroidism). Both of these

conditions have a list of side effects and both are connected to poor sleep. If you suffer from Hyperthyroidism you'll begin to show symptoms of nervousness or irritability and bouts of sweating and heart palpitations. Hypothyroidism suffers from sleep apnoea.^[16]

Resetting Your Sleep Clock and Improving Your Rest and sleeping pattern!

Manipulate Lighting Research suggests that manipulating light exposure might facilitate resetting the clock, notably for disturbances caused by jet lag. Light remains a key focus of researchers, and is commonly a point of treatment for sleep phase disorders. The daily cycles of lightness and darkness are a key “zeitgeber” or cue that acts on the mechanisms of your sleep clock and circadian rhythms. Retinal ganglion cells in your eyes notices light cycles and transmit info to your SCN.

Fast, Then Normalize Meal Times Digestion and metabolism additionally play a job in wakefulness and sleepiness. After you eat, and to some extent, what you eat, will assist you reset your sleep clock. Harvard researchers found that, circadian rhythms shifted to match food availability. Researchers recommend that fasting for about sixteen hours might facilitate reset sleep clocks for humans and reduce jetlag during traveling. For non-jetlag sleep clock disturbances, you may try a 16-hour fast. Eat early dinner (around say 4 p.m.), so avoid food till mealtime (8 a.m.) the subsequent morning.

Go Camping Since natural light schedules facilitate the body's circadian rhythm, it is sensible that spending much of the time outdoors might facilitate restore natural cycles. For your next vacation, take into account taking to the tents to reset your sleep clock. Researches published within the Current Biology journal place this hypothesis to the check; with eight participants outlay one week habitation without electrical lighting, sensible phones or laptops. They found this natural pattern helped synchronize biological clocks to solar time, with folks sleeping earlier and waking sooner than in their traditional routines. The big changes were seen in evening types, or “night owls.”

Take Gradual Steps For many folks, slow and gradual changes are best once it involves achieving long-term results. Little changes may also be easier on you physically and mentally, particularly if you don't have days to recover from sleep deficits. As an example, if your sleep clock is running late by 2 hours, here's a possible plan for obtaining back on track painlessly within one month. Each week, set your bedtime and wake time quarter-hour earlier on Sunday nights, although on Wednesdays. After four weeks, you must get back on track.^[10]

Natural Sleep Remedies

Home remedies

Warm milk: You can sip heat milk before bed. Almond milk is a wonderful supply of Ca^{+2} , that helps the brain produce melatonin.

Sleepy-time snacks: the most effective sleep-inducing foods include a mix of proteins and carbohydrates. Light snack like banana with a spoon full peanut butter, or a whole wheat cracker with some cheese. Eat any of these snacks concerning half-hour before hitting the hay.

Magnesium: It plays a key role in sleep. You'll be able to get Mg from food. Rich sources include green leafy vegetables, wheat germ, pumpkin seeds, and almonds. Visit your doctor before taking Mg supplements. Mg will act with many alternative medications, and an excessive amount of it will cause serious health problems.

Lavender: Lavender oil is calming and may facilitate encourage sleep in some individuals with sleep disorder, research shows. In order to relax your body tries taking bath with lavender oil before bed.^[30]

Valerian root: This medicinal herb has been used in treating sleep issues since history. If you are trying valerian as a sleep remedy, be patient. It will take some weeks for it to require result. Refer to your doctor before taking valerian and follow label directions.^[35]

L-theanine: This amino acid found in tea leaf leaves might facilitate combat anxiety that interferes with sleep. L-theanine reduced pulse rate and immune responses to stress. It's thought to work by boosting the quantity of a feel-good secretion your body makes. It additionally induces brain waves coupled to relaxation. Refer to your doctor before taking it.^[30]

Lifestyle Changes: Changes in lifestyle and environment may assist you combat sleep problems:

Turn off the TV. In some individuals, nighttime light will hinder melatonin hormone and make "social jetlag," to keep your sleep surroundings as dark as attainable, Moving the TV out of your sleeping room and employing a DVR or TiVo to record favorite late-night shows for later viewing.^[28]

Put different appliances to bed, too. If you want to use bedroom electronics, select those illuminated with red light that is best for sleep than blue light-weight.

Exercise early. Exercise improves sleep and overall health. The quantity of exercise and at which time of day it's done makes a difference. Researchers found that women who exercised at a moderate intensity for a minimum of half-hour every morning, seven days per week, had less trouble sleeping than women who exercised less or later within the day. Morning exercise appears to have an effect on body rhythms that have an effect on sleep quality. One amongst the explanations for this interaction between exercise and sleep could also be temperature. Your body temperature increases throughout exercise and takes up to six hours to move right down to normal. Because the cooler body temperatures are coupled to better sleep, it's necessary to provide your body time to cool down before bed.

Keep your slumber surroundings tranquil. Your sleeping room must feel like a sanctuary. Piles of garments thrown on your bed, stacks of bills watching you, or different random litter can hamper your emotion and will cause sleep issues. A tranquil and arranged area can assist you feel relaxed.

To make the proper sleep setting, strive the following:

- Don't let your sleeping room get too hot or too cold. Sleep will be discontinuous at temperatures below 54 F or on top of 72 F.
- Buy a decent pad. You pay 1/3 of your life in your bed, therefore its well worth the investment.
- Make use of a pillow to supports your head and neck. Offer the pillow the bend test: If you bend it in half and it stays in position, it's too floppy.
- To filter unwanted sounds, use a noise machine.

Your brain still hears things after you sleep. Natural sleep remedies will do wonders for the occasional bout of poor sleep. They shouldn't be used for chronic sleep issues, though, Harris says. If you've got sleep disorder that lasts for some weeks or a lot of, consult with your doctor.^[1,3,5,6,18,20,22,26,28,29,30,33,34,35]

CONCLUSION

Clocks throughout our body control ~24 hour rhythms of behavior (sleep/ wake cycle, eating patterns, physical and social activity) and physiology (hormone release, metabolism, muscle capability, attention/alertness etc.).

These are referred to as biological rhythms which are produced in almost every cell of our body and are coordinated by a specialized area of brain known as the suprachiasmatic nucleus (SCN). Maintaining robust biological rhythms is very important for our health. The importance of circadian timing has been demonstrated both through evolutionary relevance and observed health implications of disrupted clock systems. Light affects the master clock (SCN) by resetting it in our brain. Biological rhythm disruption is caused by erratic behavior or by conflicting timing of our internal rhythms and our environment (such as light and food). Disrupted biological rhythms can have negative impacts to health including increased risk for cardiac diseases, cancer, diabetes, obesity, sleep disorders, and depression etc. We can maintain a healthy clock by eating within 10-12 hours/day, getting exposure to sunlight in the mornings, trying to go to bed and wake up at the same time each day and exercising regularly but not too late.

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