

Milk-Hormones: Narrative Review

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Received date: September 17, 2018; Accepted date: September 19, 2018; Published date: September 30, 2018

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Abstract

Milk is the major source of nourishment for newborn mammals prior to the other types of food. The composition of the cow's milk widely varies between the different breeds and also during the different stages of lactation. Milk from animals contains fat, carbohydrates, vitamins, proteins, minerals and water. Water is the main constituent of milk which dilutes the milk and allowing its secretion from the body. Milk is the secretion of Mammary glands; hence it consists of constituents from the blood plasma, accordingly hormones that are transported in blood may be detectable in milk. The importance of hormones was discussed about decades back but still there are more concerns to look at the hormones as biomarkers in some serious problems and during pregnancy. In recent research, it has been found that further property of hormones in dairy items has conceivable effect on human wellbeing including the part of a few estrogens and insulin-like development factor which leads to bosom, prostate and endometrial tumors. Dairy animals' normally contains various steroid and protein (peptide) hormones in minute quantities. The most critical hormones found in milk and other dairy items which are identified by diagnostic techniques comprises of prolactin, steroids including estrogens, progesterone, corticoids, and androgens. Additionally, the presence of different hormones, for example, insulin-like development factor-1 (IGF-1) and neighborhood hormones including prostaglandins (PGs), in dairy items has been accounted for. It has been expected that a large portion of the hormones are moved into milk by dissemination. In this review we concentrated on several aspects of presence of hormones in dairy foods with especial emphasize on cow's milk as a major source of consuming milk for humans.

Introduction

The cows which produce milk are may be pregnant, fed and raised organically, etc. or maybe not. Considering these things alone, it cannot be predict that cow's milk is Hormone-Free milk, because cow's milk contains about 60 different hormones naturally without integrating anything to it (Figure 1). Though everyone has different hormone situations, there are no proper studies regarding the need to take integrated hormones from another mammal.

Dairy products additionally include hormones which could result in mood swings due to the presence of Estrogen. Testosterone and Estrogen are the intercourse hormones, and after they get out of balance in line with our bodies desires, we go through mood swings as an end result.

Dairy milk promotes excess estrogen within the frame because of it containing estrogen from female cows. On the same time, milk obviously includes androgenic residences, so it increases testosterone in the body and can purpose bulking quickly.

Despite the fact that eating milk increases your estrogen level slightly, most healthful people do not enjoy the ill effects from eating slight quantities of dairy products. Milk is a terrific source of calcium, nutrition D and protein.

Soy milk additionally affords protein and is often fortified with nutrients and minerals. Before appreciably changing the milk intake, communicate for a physician to make sure it's far safe for oneself.

Steroid Hormones

- 5- α Androstane-3,17 dione
- Corticosterone
- Estradiol
- Estriol
- Oestrone
- Progesterone
- Vitamin-D

Growth Factors

- IGF - binding proteins
- MDGI
- TGF- β

Hypothalamic Hormones

- Luteinizing hormone - releasing hormone
- Gonadotropin hormone - releasing hormone
- Somatostatin
- Thyrotropin - releasing hormone

Pituitary Hormones

- Growth hormone
- Prolactin

Others

- PGF α
- Transferin
- Thyroxin (T3 and T4)
- Gastrin - releasing hormone

Figure 1: Milk hormones.

Prolactin (PRL)

Prolactin (PRL) is a polypeptide hormone which is also called as luteotropic hormone or luteotropin. PRL is a protein which enables mammals, usually female are in milk secretion [1] from the breast after estrogen and progesterone priming. After the placental expulsion during the time of child birth, there is sudden and unexpected

decrease in the circulation of progesterone and estrogens. This decrease in the level of estrogen initiates lactation [2]. Both estrogen and prolactin work together in the growth of breast but estrogen antagonizes the milk-producing effect of PRL on the breast. In addition, prolactin makes the way for the maternal behavior. Prolactin is released from the front pituitary organ in light of milking boosts and suckling during the lactation period. Furthermore, the couplomimetic boost to the cervix amid copulation is likewise named physiological jolts for PRL discharge. The release of prolactin is not limited to the front pituitary organ as some different tissues and organs, for example, amygdala, cerebrum stem, hippocampus, hypothalamus, septum, spinal rope and telencephalon, indicated ability of prolactin blend in creature considers [3]. There is no notable distinction in the prolactin of the cow's milk. The best-settled destinations of PRL activity in warm blooded creatures incorporate the mammary organ and ovaries, notwithstanding, PRL restricting locales have been recognized in different parts of the body, for example, CNS, pituitary organ, heart, lung, thymus, spleen, liver, pancreas, kidney, adrenal organ, uterus, skeletal muscle and skin. The Lactogenesis, direction of ovarian and testicular capacities, commitment in conceptive and parental practices, angiogenesis, homeostasis of the invulnerable framework and osmoregulation are the outstanding elements of the prolactin.

Prostaglandins

Prostaglandins are the lipid mediators, which are formed from the Arachidonic acid found in most of the organs and tissues. This Arachidonic acid by the help of the enzyme PGHS (Prostaglandin H Synthetase) is converted to Prostaglandin H₂ which act on the endothelium and mast cells. At certain stage of infection prostaglandin production will increase [4].

Certain research shows that during the last pathway of the uterine parturition and contractility [5], these prostaglandins are involved. Prostacyclins, which is the member of prostaglandins present at the time of early pregnancy. Prostacyclins also known as prostaglandin I₂ (PG I₂) which dilate the blood vessels and hence it is responsible for the uterine quiescence at time of pregnancy. A study shows that even though the prostaglandins are processed in the fetal membrane and placenta, they might not be necessary for labour in knock-out mouse. Within uterus, before and all through the labour the prostaglandin tiers are improved. Prostaglandin F₂ alpha (PGF₂ α), which is a type of prostaglandin occur naturally with the aid of maternal decidua. They act at the middle of the uterine wall (myometrium) and thereby induce the urine contractions. Prostaglandin F₂ is very important for softening of the cervix. Softening of the cervix (Cervical ripening) are related to cervical dilation, degradation of the collagen and spontaneous rupture of the fetal membranes. There are many elements which are influenced due to the prostaglandins production. These effects are accelerated and decelerated with help of estrogen and progesterone respectively.

Steroid hormones

When a steroid acts as a hormone it is called as the steroid hormone. These hormones helps in improving the efficiency of feed conversion and they also promote the animal growth. Steroid hormones include Androgens, Estrogens, Progesterone and other related compounds [6]. These hormones are originated from the blood flow, pass within the mammary gland and secreted into the milk. Certain hormones can also be produced by the mammary gland and then it is transfer into the milk.

Since along these lines there is no uncertainty about the current of them in drain, as the nearness of steroid hormones particularly progesterone content in drain is utilized as an analytic toll of pregnancy. Early investigations demonstrated that the principle estrogen in dairy animals' drain is the naturally inert 17β-estradiol, which took after by estrone and 17β-The nearness of 17β-oestradiol, estrone-and estriol-sulfate in human bosom sore liquid has just been illustrated [7].

Estrogens

Oestrogen or Estrogen mainly presents in females and it is responsible for characteristics, regulation and development of the female reproductive system. During puberty, the ovaries begin releasing estrogen hormones in line with each monthly menstrual cycle. The estrogen level rises suddenly halfway through the cycle, which triggers the release of an egg. This level then quickly decreases after ovulation. Generally, estrogens levels affects the physiological functions [8] which includes, low level of estrogen content may increase the risk of chronic diseases and high level of estrogen exposure can also damages the health of the individual.

The Estrone (E1) and Estradiol (E2) are the active estrogens in the non-pregnant women and Estriol is the active estrogen in the pregnant women. Studies show that men also naturally produce estrogen in minute quantities [9]. Although the role of estrogen in male is not clear, it has been said that estrogen regulates the luminal fluid present at the epididymis.

When compared to the non-pregnant cows, pregnant cows Estrogen levels in milk will be 20 times higher. It has been consider that intake of elevated amount of estrogen could lead to risk of certain type of cancers. But certain study shows that intake of milk from a pregnant cow did not raise plasma levels of E1 and E2 in mice.

Progesterone

Progesterone is important for pregnancy support and direction of the estrous cycle. Progesterone assumes a basic part in empowering generation of an assortment of endometrial discharges that are important for effective embryonic advancement. Early embryonic misfortune ranges from 20% to 30% amid the initial 30 d of growth in dairy cattle. Progesterone is created by the corpus luteum (CL) on the ovary which shapes after ovulation of the oocyte [10]. Progesterone targets uterine epithelium, mammary tissue, myometrium and hypothalmus causing endometrial discharge, hindrance of GnRH discharge and advances support of pregnancy.

The level of progesterone in the serum and drain mirrors the action of the CL on the ovary. The level of progesterone increments for the initial 4 to 6 days following ovulation. Most extreme levels are come to between days 10-17.

In the event that the bovine winds up pregnant, the CL is kept up and elevated amounts of progesterone are created which looks after pregnancy. In the event that the dairy animals does not wind up pregnant [11], the CL starts to relapse and the level of progesterone strongly diminishes on days 18 or 19 and enabling the cow to profit to estrus for day 21-23.

The drain Progesterone focus was brought down in dairy animals, which nourished by abnormal state of think and the conceivable translation for that diminishment was an outcome of expanded metabolic leeway of progesterone related with expanded vitality

admission. It has been discovered that the drain aggregate progesterone focus amid the third luteal stage baby blues was higher for dairy animals with low drain yields.

Recombinant bovine somatotropin (rbST)

Recombinant cow-like development hormone (rBGH) or recombinant cow-like somatotropin (rbST) alludes to cow-like development hormone that is made in a lab utilizing hereditary innovation. Some rBGH items available contrast artificially from a bovine's common somatotropin by one amino corrosive. Both the common and recombinant types of the hormone empower a dairy animals' drain generation by expanding levels of another hormone known as insulin-like development factor (IGF-1). rBGH-treated dairy animals has larger amounts of IGF-1, a hormone that ordinarily causes a few sorts of cells to develop. A few investigations have discovered that IGF-1 levels at the high end of the ordinary range may impact the improvement of specific tumors. As a matter of first importance, rbST is species-particular, which implies that bST isn't naturally dynamic in people, regardless of whether infused. bST is a protein which is separated to amino acids and peptides in the gastrointestinal tract, and thus, are segments which have no hormonal action. Additionally, sanitization devastates 90% of bST in drain [12]. Moreover, any follow measures of bST ingested in drain are separated into idle parts (i.e., constituent amino acids) by chemicals in the gastrointestinal tract, much the same as some other protein. All drain contains minute measures of bST paying little mind to whether from untreated dairy animals or cows treated with rbST [13].

Vitamin C

Vitamin C is useful in the production of Progesterone, which is an anti-depressant and anti-anxiety hormone. Citrus fruits, tomatoes, strawberries, kiwi, bell peppers are some of the food sources of vitamin C. Since Vitamins are relatively unstable and their activity in foods depends on pH and their stability to heat, light, oxygen, oxidizing agents and enzymes. In recent research, to improve the nutrient content of foods [14], Vitamins and minerals fortification are been used. Recent advances in the techniques of microencapsulation for the flavouring of milk with vitamin C which provide higher shelf life and also stable vitamin C which can be a good asset to fortify with foods. Hence, flavoured milk is selected based on the stability in the ambient conditions and also one of the good vehicles for supplying the vitamin C and other milk constituents of milk [15].

Since vitamin C is helpful in the production of Progesterone and estrogen. The consumers are subjected to excess of estrogens although the Dairy products naturally contain estrogens. Hence excess production of these Estrogen and Progesterone can cause adverse health effects.

Androgens

Androgen is a steroid hormone which balances the maintenance and growth of the male reproductive system by binding to androgen receptors. Studies show that the main source of androgens is the testes. But certain studies prove that testosterone and androgens are present in cow's milk [16]. Mainly Androstenedione (5 α -androstane-3, 17-dion), a naturally occurring steroid hormone is present about 1 to 5 ng per mL of milk. The study also mentions about the Androstenedione hormone can be produced by either within the part of mammary gland or in the adrenal glands, which indicates the 5 α -steroids positions in

lactogenesis. Certain studies shows that Androstenedione concentration in the milk and plasma were increased during the time of pregnancy, but this amount of increase is as double the times of plasma after 90 days [17]. But, earlier studies show that the androgens in milk not likely to produce certain biological effects in milk customers.

Androgen or testoids or androgenic hormone was discovered in the year of 1936, it is a Steroid hormone which controls or stimulates the characteristics of the male attributes in humans by binding to the NR3C4, a nuclear receptor. NR3C4 is also called as (AR) [18]. The characteristic of the masculine attributes includes the activity of the male sex organs and also male secondary sexual characteristics. Androgens are the forerunner of all the estrogens, the female sex hormones. There are many androgens known in which the well-known and most important androgen is Testosterone. Other members of the androgens and their functions are tabulated in the Table 1.

Androgens	Functions
Dehydroepiandroster (DHEA)	Primary precursor of the estrogen
Androstenedione (Andro)	Stimulation of Estrogen
Androstenediol	Regulates gonadotropin secretion
androstenediolglucuronide	Regulates gonadotropin secretion
Androsterone	Stimulates masculine characteristics
Dihydrotestosterone (DHT)	Development of male reproductive tissue

Table 1: Androgens and their functions.

Many studies show that estrogen and progesterone plays the potential role at the time of birth. But the studies related to the androgens during pregnancy and at the time of birth are relatively less. This review also shows the importance of the androgen and its functions during the pregnancy and at the time of birth. One of the main functions the Androgen hormone, is during the gestation period. Throughout the gestation period, the androgen levels are likely to be increased for the maintenance of pregnancy and initiation of birth [19]. The study shows that only some androgens are increased throughout the gestation period in maternal circulation. Although this study is not fully understood, but the key point to note is that the androgens are important during the pregnancy and initiation of birth. This may also lead to the development of new salubrious approaches to manage pregnancy difficulties such as premature birth [20].

Another study shows that the androgens are also helpful in the simulation of the myogenesis process for the formation of muscular tissue. The exact type of cells are not yet known for the simulation within the human skeletal muscle because the testosterone promotes the commitment of pluripotent, mesenchymal cells into myogenic lineage [21-23], it has been said that that Androgen Receptor (AR) would be expressed in mesenchymal precursor cells in the skeletal muscle. After certain observations, it has been believe that androgens increase muscle mass in part by acting on several cell types to regulate the differentiation of mesenchymal precursor cells in the skeletal muscle.

Corticoids

Corticoids or Corticosteroids are the class of the steroidal hormone present in the milk. Corticoids involved in the lactogenesis process with other hormones. Adrenocorticotrophic hormone-ACTH controls the release and synthesis of the hormone and the corticoids are produced in the adrenal gland. Corticosteroids are taken up from the blood [24]. The mammary gland of goats and cows takes the corticosteroids from the blood. Ranges of corticosteroids in milk varies from human to cow, while comparing the levels it has been found that cows contains low levels of corticosteroids from 8 ng/ml to 18 ng/ml when compared to human [25].

Ranges of corticosteroids vary between cow and human. A study shows that human produce more corticosteroids of about 20-136 ng/ml when compared to cow (8-18 ng/ml).

Another study shows that the use of dexamethasone, a glucocorticoid medication used in the treatment of many diseases in other animals. Adrenal gland disorder can be tested by using this synthetic corticoid. In a particular study it has been said that the treatment of the Holstein cows with the adrenocorticotrophic hormone increases the milk cortisol level four times than the normal [26]. This is because of the prolong increase in the plasma cortisol level. Corticoids levels in the milk may also elevate due to certain stressful conditions such as diet changes, transport, environmental conditions such as temperature changes, neuronal diseases, etc. Corticoids are oxidised and reduced in the liver and excreted *via* urine. By using the Comparative Protein Binding (CPB) method, quantification and the detection of the corticoids have been performed and also different analytical methods are used to quantify the corticoids concentration in the milk products [27]. GC-MS (Gas Chromatography- Mass Spectrometry) and LC-MS (Liquid Chromatography-Mass Spectrometry) techniques are used for the determination of the corticoids in milk quantitatively. Methods such as immune enzymatic assay and ELISA (Enzyme-linked Immunosorbent Assay) Link are also used to determine the corticoids in the milk. In spite of all these research regarding the quantification and the detection of corticoids in milk [28-31], there is still insufficiency of the knowledge of the biological effects and the absorption of corticoids in milk of both animals and humans.

Conclusion

The information we gathered in this review paper are from the articles which are published in the Science-Direct, NCBI and from Google Scholar. This review is mainly focused on the hormones in dairy products or foods and its biological effects in both humans and animals. With the information provided we can conclude that dairy products should be taken into concern for producers, consumers and public health ascendant entities. We also summarized about the biosynthesis and metabolism of certain hormones. In summary, it is a thought of concern about the health of the consumers due to some current issues regarding the dairy food hormones and it is also necessary to clarify the impacts in the dairy products hormone content.

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