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Review

Modulation of prostaglandin synthesis to improve farm animal reproduction

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ABSTRACT

Prostaglandins are biomolecules made of 20-carbon unsaturated hydroxyl fatty acids with a cyclopenta ring; PGE2 and PGF2alpha are the two prostaglandins that are most crucial for animal reproduction. While PGE2 exhibits strong luteotropic and luteoprotective qualities, PGF2alpha is known to be a potent luteolytic and ecbolic in action. Nutrition and hormones can be used to modify prostaglandin synthesis and release from the body. The primary fatty acids important for animal reproduction are long-chain n-3 fatty acids like eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) as well as long-chain n-6 arachidonic acid (AA). While pasture or forage, vegetative cereals like silage, linseed or flaxseed are a good supply of short chain n-3 alpha-linolenic acid, grains, soybean meal, soybean, sunflower and olive oil are excellent sources of short chain n-6 linoleic acid. It has been demonstrated that feeding n-3 PUFA-rich meals can improve farm animal fertility in a number of ways, including by lowering the PGF2alpha-PGE2 ratio. In order to reduce the formation of PG in sheep, cows and pigs and boost the reproductive efficiency of the animals, meals with the proper ratio of n-3 PUFA and n-6 PUFA can be used for a number of objectives.

Keywords: Prostaglandins; farm animals; reproduction; eicosapentaenoic acid; docosahexaenoic acid

INTRODUCTION

Prostaglandins were identified in mammalian semen and were considered to have originated from the prostate gland, hence their name. They are among the body's most prevalent and active physiological chemicals (Senger 2003).

Prostaglandins are biomolecules composed of cyclopenta-ringed 20-carbon unsaturated hydroxyl fatty acids. They are generated from arachidonic acid and at least six biochemically active prostaglandins have been found as well as several metabolites. PGE2 and PGF2alpha are the two most essential prostaglandins in animal reproduction. These two biomolecules are involved in many functions, including luteolysis, ovulation, uterine contraction, pregnancy identification and maintenance (Senger 2003).

Structure (Figs 1-3): Arachidonic acid is synthesised from phospholipids by the enzyme phospholipase A2. AA then passes via the cyclooxgenase pathway producing thromboxane, prostacyclin and prostaglandin E, D and F. PGE2 is produced by the enzyme prostagladin E synthase which acts on PGH2. Similarly, the enzyme prostglandin F synthase acts on PGH2 to produce PGF2alpha (Weems et al 2006).

Throughout the estrous cycle, the bovine endometrium secretes PGE2 and PGF2alpha, although the secretory pattern is distinct. Days 15-17 are thought to be a crucial time when luteolysis begins due to an

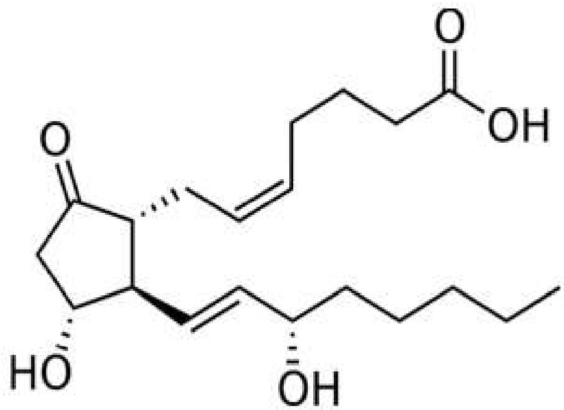

Fig 1. Structure of PGE2

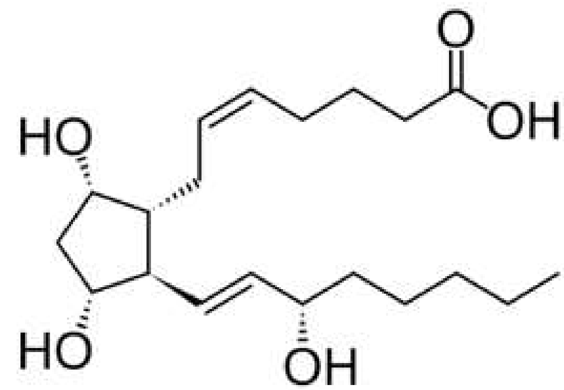

Fig 2. Structure of PGF2alpha

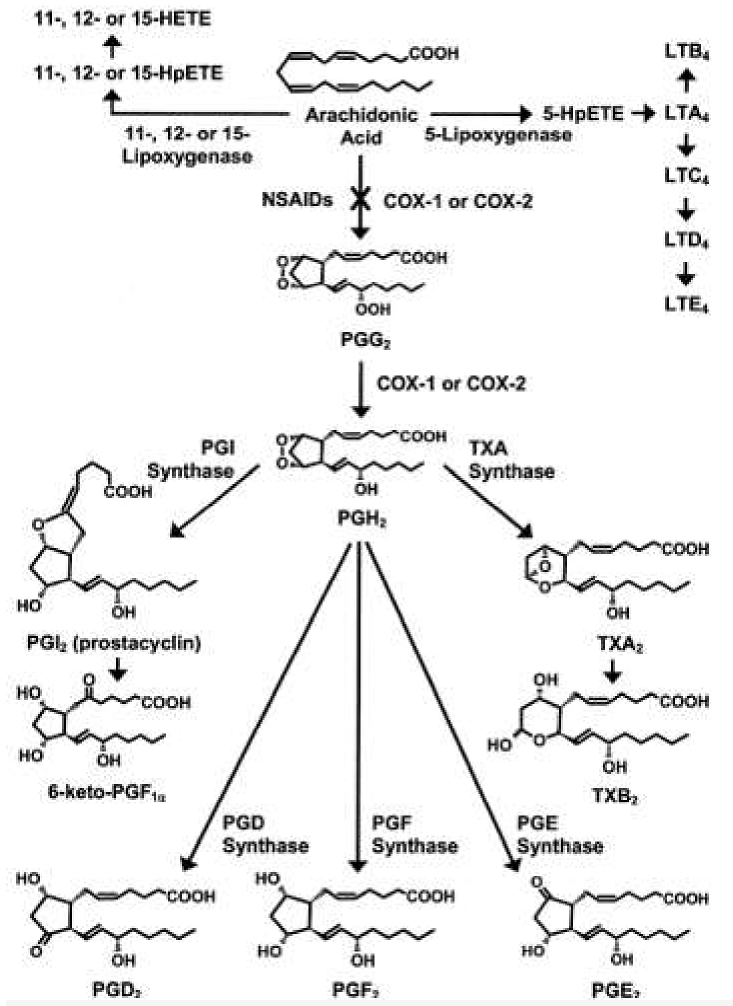

Fig 3. Formation of PGH2 and PGF2alpha

increase in PGF2alpha secretion when there is no viable embryo present. On the other hand, it has been demonstrated that PGE2 production by the endometrium is higher in cattle during the mid- and late-luteal phases of the estrous cycle. PGE2 is a crucial mediator in endometrial receptivity, myometrial quiescence and immunological activity during the development of pregnancy. It has been demonstrated to have luteotropic and luteoprotective properties (Weems et al 2006).

The release of oxytocin, which is primarily produced by the CL, which contains secretory granules similar to those in the posterior pituitary and the activation of uterine oxytocin receptors, both influence the release of PG. Increased OT pulses are synchronised with PGF2alpha metabolite pulses (Weems et al 2006). It has been established that the relative ratio of PGE2 and PGF2aplha secretion is more significant than their individual absolute concentrations. In the middle and late luteal phases, the PGE2-PGF@alpha ratio rises, which increases PGE2's impact. This ratio falls as luteolysis begins because PGF2alpha begins to affect the CL at the beginning of the follicular phase. PGE2 is converted to PFG2alpha by the enzyme PGE 9-ketoreductase and various chemicals, including IL-1, TNF alpha and NO, which are thought to be mediators of PG biosynthetic regulation, have an impact on this enzyme's activity. Furthermore, it has been demonstrated that these cytokines have a direct impact on progesterone production, luteolysis and PG release.

Therefore, prostaglandins have a significant role in the physiology of animal reproduction and their manipulation may affect the reproductive efficiency of farm animals. According to a number of studies, giving n-3 polyunsaturated fatty acids (PUFA) to ruminants and pigs has a positive impact on these animals' reproductive performance in terms of their ovulation rate, cyclicity and conception rate. These outcomes are a consequence of PUFA modulating PG production in farm animals. Similarly, research on giving phytoestrogens to agricultural animals, notably ruminants, has revealed that they can alter prostaglandin production and affect reproductive performance.

Modulation of PG synthesis by dietary feeding of n-3 and n-6 PUFA in farm animals

Long-chain n-3 fatty acids like eicosapentaenoic acid (EPA), docosahexaenoic acid (DHA) and long-chain n-6 arachidonic acid (AA) are the main fatty acids of importance in animal reproduction. Through a series of stages involving desaturation and elongation, the body creates these long-chain polyunsaturated fatty acids (PUFA) from the short-chain n-3 alpha-linolenic acid (ALA) and n-6 linoleic acid (LA). Animals are unable to synthesise the short-chain ALA and LA, hence they must be obtained through diet. Ruminants convert ALA and LA to long-chain fatty acids and levels of ALA and LA in the diet have an impact on the levels of n-3 in reproductive tissue (Cheng et al 2001).

While grains, soybean meal, soybean, sunflower and olive oil are rich sources of short chain n-6 linoleic acid, pasture or forage, vegetative cereals like silage, linseed or flaxseed are a strong source of short chain n-3 alpha-linolenic acid. Fish meal, fish oil and algae are sources of long chain n-3 EPA but they are pricey. In ruminant diets, there aren't many sources of long-chain n-6 AA (Gulliver et al 2012).

Prostaglandins (PG), particularly PGE2 and PGF2alpha, which are crucial PGs involved in animal reproduction, are synthesized from the long-chain PUFAs EPA and AA. Long chain n-3 EPA supplementation has been reported to suppress PGF2alpha release, however, the precise mechanism is unknown. By serving as cyclooxygenase substrates, competitive inhibitors of cyclooxygenase, which prevent the AA from being available for metabolism and competitive inhibitors of PGH synthase action on AA to convert to PGH2, the n-3 may have an impact on PG synthesis. When calculating the impact on PG production, the ratio of n-6 to n-3 in the diet matters more than the absolute value (Gulliver et al 2012, Wathes et al 2007).

The effects of n-3 fatty acid supplementation on farm animal fertility are explained in the following ways:

1) It is hypothesised that the high concentrations of PUFAs in the plasma membrane of the oocytes of several farm species are taken up by the oocyte cells in a selective manner. It has been demonstrated that n-3 fatty acid-rich diets are advantageous for oocyte maturation, fertilisation and subsequent differentiation (Mahla et al 2017, Gulliver et al 2012, Wathes et al 2007).

2) Cows fed such diets have earlier estrus onsets because n-6 rich diets have been demonstrated to promote luteal regression. On contrast, estrus onset is delayed and the length of the estrous cycle is prolonged on diets high in n-3 fatty acids (Mahla et al 2017, Gulliver et al 2012, Wathes et al 2007).

3) When consumed after insemination, n-3-rich diets have been proven to increase conception rates, lengthen gestations and reduce the likelihood of

miscarriages. This might be as a result of n-3 diets' ability to suppress PGF2alpha secretion and stop luteolysis (Mahla et al 2017, Gulliver et al 2012, Wathes et al 2007).

4) N-6-rich diets have been demonstrated to raise PG levels in sheep and cows, which increase the risk of miscarriage (Gulliver et al 2012).

5) Diets high in n-3 have been linked in pigs to larger litters and higher foetal survival rates in succeeding gestations. Additionally, when PUFAs are present in the mother's diet, the piglets' tissue is enriched with them, which enhances their behaviour and increases their survivability. However, the studies mainly used animal or plant-based oils as source of n-3 PUFA (Malm et al 1976, Tanghe and De Smet 2013).

Therefore, meals with the right proportion of n-3 PUFA and n-6 PUFA can be utilised for a variety of purposes to control the PG production in sheep, cows and pigs in order to increase the reproductive effectiveness of the animals.

Modulation of PG synthesis by dietary feeding of phytoestrogens in farm animals

Soy-phytoestrogen is the main example of phytoestrogens, which are estrogenic compounds originating from plants. They are well-known for having positive impacts on people, including lowering the risk of cardiovascular disease, breast cancer and serving as antioxidants. It is also known that cows who consume heavy phytoestrogen feed can become infertile (Woclawek-Potocka et al 2005b). The endogenous oestrogens have a regulatory effect on PGF2alpha release and phytoestrogens can serve as agonists or antagonists of these hormones. PGF2apha is known to be released more readily in farm animals when oestrogen is present (Woclawek-Potocka et al 2005a).

Daidzein and genistein, two commonly found phytoestrogens in soy, are converted by ruminants into equol and para-ethyl-phenol respectively (Woclawek-Potocka et al 2006). These are present in large amounts in cows fed diets high in phytoestrogens. Although phytoestrogens have a limited affinity for binding to oestrogen receptors, their comparatively large plasma concentrations make up for this and cause infertility. Equol and p-ethyl phenol, two phytoestrogen metabolites, also exhibit higher binding affinity than crude phytoestrogens, which contributes to the negative effect. This alters the PGE2-PGF2alpha ratio and causes an increase in PGF2alpha pulse secretions (Woclawek-Potocka et al 2006) Therefore, phytoestrogen-rich diets in cows impair CL function, embryo implantation and development as well as mother awareness of pregnancy.

However, they only slightly boost PGE2 secretion from both stromal and epithelial cells. Phytoestrogens and their metabolites preferentially promote PFG2alpha release from endometrial epithelial cells rather than stromal cells. In contrast, only epithelial cells are stimulated by endogenous oestrogen to release PGF2alpha and PGE2. Additionally, phytoestrogens and their metabolites stimulate PGF2alpha more strongly than the PGE2. This suggests that when these drugs are present in high plasma concentrations and have negative reproductive effects, they increase the release of PGF2alpha. (Woclawek-Potocka et al 2005a).

In order to prevent negative reproductive consequences including pregnancy failure and pregnancy loss, the diets supplied to animals, especially after insemination, should be checked to ensure that very low or zero amounts of phytoestrogens are present. Additionally, it is best to steer clear of feeding farm animals meals high in phytoestrogens because doing so raises the plasma PGF2alpha concentration, which in turn causes infertility and anestrous condition because the CL cannot be maintained under such circumstances (Woclawek-Potocka et al 2005b).

Modulation of PG synthesis by progesterone (Silvia et al 1991)

Early progesterone administration during the estrous cycle causes premature PGF2alpha secretion, which leads to luteolysis. On the other hand, giving a progesterone receptor antagonist during the initial half of the estrous cycle delays the beginning of PGF2apha secretion and luteal regression. As a result, changing the time that the uterus is first exposed to progesterone affects the time that PGF2alpha pulsatile secretion starts.

Prostaglandin removal can also result in early PGF2alpha release. Progesterone has an impact on oxytocin's uterine secretory responsiveness, which is necessary for the positive loop of PGF2alpha pulse release. To suppress and stimulate the release of prostaglandins, progesterone and progesterone antagonists like progesterone controlled internal drug release respectively can be employed as medications.

CONCLUSION

Prostaglandins, specifically PGE2 and PGF2alpha, are necessary for optimal reproductive system function in agricultural animals. Their spectrum of activity is very broad, including luteolysis, ovulation, pregnancy detection, pregnancy maintenance and parturition. Modulation of prostaglandin synthesis and release from the body can be accomplished through nutrition and hormones. Feeding n-3 PUFA rich meals has been shown to promote fertility in farm animals in a variety of ways, including reducing the PGF2alpha-PGE2 ratio and, thereby, improving farm animal fertility. Furthermore, phytoestrogen-rich diets have been proven to have a negative influence on the reproductive system by increasing PGD2alpha production, hence their concentration in feeds must be managed. Finally, because progesterone modulates PGF2alpha release in the body, its exogenous treatment may be used to modulate PGF2alpha release and improve reproductive efficiency in animals.

REFERENCES

Cheng Z, Robinson RS, Pushpakumara PG, Mansbridge RJ and Wathes DC 2001. Effect of dietary polyunsaturated fatty acids on uterine prostaglandin synthesis in the cow. Journal of Endocrinology **171(3):** 463-473.

Gulliver CE, Friend MA, King BJ and Clayton EH 2012. The role of omega-3 polyunsaturated fatty acids in reproduction of sheep and cattle. Animal Reproduction Science **131(1-2):** 9-22.

Mahla AS, Chaudhari RK, Verma AK, Singh AK, Singh SK, Singh G, Sarkar M, Dutta N, Kumar H and Krishnaswamy N 2017. Effect of dietary supplementation of omega-3 polyunsaturated fatty acid (PUFA) rich fish oil on reproductive performance of the goat (*Capra hircus*). Theriogenology **99:** 79-89.

Malm A, Pond WG, Walker EF Jr, Homan M, Aydin A and Kirtland D 1976. Effect of polyunsaturated fatty acids and vitamin E level of the sow gestation diet on reproductive performance and on level of alpha tocopherol in colostrum, milk and dam and progeny blood serum. Journal of Animal Science **42(2):** 393-399.

Senger PL 2003. Pathways to pregnancy and parturition. 2nd Edn, Current Conceptions, Inc, Pullman, WA.

Silvia WJ, Lewis GS, McCracken JA, Thatcher WW and Wilson L Jr 1991. Hormonal regulation of uterine secretion of prostaglandin F2 alpha during luteolysis in ruminants. Biology of Reproduction **45(5):** 655-663.

Tanghe S and De Smet S 2013. Does sow reproduction and piglet performance benefit from the addition of n-3 polyunsaturated fatty acids to the maternal diet? Veterinary Journal **197(3):** 560-569.

Wathes DC, Abayasekara DR and Aitken RJ 2007. Polyunsaturated fatty acids in male and female reproduction. Biology of Reproduction **77(2):** 190-201.

Weems CW, Weems YS and Randel RD 2006. Prostaglandins and reproduction in female farm animals. Veterinary Journal **171(2):** 206-228.

Woclawek-Potocka I, Acosta TJ, Korzekwa A, Bah MM, Shibaya M, Okuda K and Skarzynski DJ 2005a. Phytoestrogens modulate prostaglandin production in bovine endometrium: cell type specificity and intracellular mechanisms. Experimental Biology and Medicine (Maywood) **230(5):** 326-333.

Woclawek-Potocka I, Bah MM, Korzekwa A, Piskula MK, Wiczkowski W, Depta A and Skarzynski DJ 2005b. Soybean-derived phytoestrogens regulate prostaglandin secretion in endometrium during cattle estrous cycle and early pregnancy. Experimental Biology and Medicine (Maywood) **230(3):** 189-199.

Woclawek-Potocka I, Bober A, Korzekwa A, Okuda K and Skarzynski DJ 2006. Equol and para-ethyl-phenol stimulate prostaglandin F(2alpha) secretion in bovine corpus luteum: intracellular mechanisms of action. Prostaglandins and Other Lipid Mediators **79(3-4):** 287-297.