

PhD Project Advertisement

Project title: Cows, cannabinoids and terpenes; screening hemp-derived compounds for anti-inflammatory properties to tackle inflammatory disorders of the dairy cow

Project No: FBS2024-030-Nash-ar

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Project description:

With a rapidly growing human population there is a global imperative to drastically increase food production and innovative farm-based solutions are required to address this need. The dairy industry is a major contributor to healthy human diets and in turn requires healthy cows for efficient milk production, maximising farm income. However, the high milk-producing dairy cow faces several health challenges immediately and sometime after calving which leads to poor fertility. Sub-fertility delays conception and therefore birth of the next calf and as a result, also delays lactation, causing substantial loss of income for farmers and reduced milk production from the farm. The challenges that cows face after calving include, depleted energy stores due to the substantial metabolic cost of producing milk early in lactation, leaving the animal with a compromised immune system and less able to resist bacterial infections. Indeed, bacterial infections and inflammation is common during this life stage, including of mammary (mastitis) and uterine (endometritis) tissues. These infections impact negatively on wellbeing, health, and fertility and consequently milk production. Existing treatments for tackling mastitis and uterine inflammation are reliant on repeat antibiotic administration, yet once bacteria are killed by the initial dose, inflammation may persist which is unresponsive to further antibiotic medication. Current anti-inflammatory products aim to break persistent inflammation but interfere with endogenous reproductive hormones, exacerbating fertility problems. No new treatment options have become available in many years. Therefore, it is a necessity to source novel, efficacious, non-antibiotic compounds. A successful candidate treatment will therefore, increase milk production per cow, reduce culling rates of sub-fertile cows, improve farm economics, and thus secure global, sustainable milk supply.

Hemp plant-derived products, such as cannabinoids and terpenes are currently enjoying much interest for their potential as anti-inflammatories, both in popular science media and as the focus of specific academic studies. For example, cannabidiol has been assessed for treating conditions including arthritis (Lowin, Ren et al. 2020) skin diseases (Nickles and Lio 2020), and intestinal inflammation (Naftali 2020). However, the utility of cannabinoids to specifically and potentially treat post-partum related inflammatory conditions of dairy cows has not been investigated. Our industrial partner, TTS Pharma, provide high quality, traceable and legal cannabinoids and terpenes available to this study.

The aim of the study is:

1. Screen specific cannabinoid and terpene mixtures (advised by TTS Pharma) for anti-inflammatory properties using a laboratory-based model. Using cells harvested from whole blood that represent the wider immune system we will simulate bacterial inflammation in these cells, and then test whether the cannabinoid-terpene mixtures can dampen the immune response, characteristic of an anti-inflammatory effect;
2. To assess the effect of the hemp compounds used in (1) on inflammatory response in whole blood from cows at different stages of lactation. For this blood from cows of known background will be used, and will include a subset of animals who have been diagnosed with metritis post-calving. This will evaluate the effectiveness of the compounds in a more characterised environment.

Based on results of previous our studies where cannabinoids and terpenes demonstrated anti-inflammatory properties specifically towards chronic endometritis, we hypothesise that these compounds will exert anti-inflammatory effects on a systemic level, represented by bovine-specific blood-derived immune cells. This early-stage drug discovery project will strengthen the evidence base for hemp-derived products to be efficacious across a number of different inflammatory conditions of the uterus and mammary gland.

The project encompasses both novelty and impact. The study is innovative in using plant-derived natural products, to combat inflammatory diseases that have received no new interventions for many years, and therefore, remains an important problem for dairy farmers and vets to resolve. Working towards improving the treatment of post-partum inflammatory disorders of the dairy cow will save treatment costs, reduce number of antibiotic treatments, adding to the veterinary surgeons tool kit. Fewer cows will exhibit long-term subfertility, reduce culling costs and maintaining animals in the breeding herd for longer, as such enhancing animal welfare and reducing farm costs. Therefore, this project has multiple benefits to producers, through a more efficient milk production chain and in turn, improved sustainability of milk production, delivering improved nutrition and health for society.

Training opportunities:

1. This project offers a unique opportunity to develop skills and competency in cell culture techniques, Luminex multiplex protein assays. Training in data handling and statistical analysis is also available at both institutes. Supervision and training will be shared by AU and the UoR, both offering comprehensive Researcher Development Programmes, including taught research skills courses, development workshops and activities to gain skills required for a career in research.
2. Science communication: The student will receive supervisory training in academic scientific communication, e.g., publication writing, conference presentation styles. Attendance and presentation at departmental seminars and national conferences will be encouraged, as will engagement with stakeholders and the wider public.
3. Opportunities for industry communication will be provided with our links to the Welsh Government initiative, Farming Connect (Farming Connect - helping you drive your business forward | Farming Connect (gov.wales)) which is based at Aberystwyth University's Innovation campus.
4. Time spent at TTS Pharma give unique insight to the running and management of a small pharma within the industry that controls an entire pipeline of production from farm to consumer. Importantly, these products are traceable, legal and pure to confer consumer confidence and conveys the importance of business integrity.

Student profile:

Applicants should hold, or expect to obtain, an upper-second class honours degree or higher in biological or animal sciences or related subjects. Applicants with practical experience in cell biology are particularly welcome. An interest in animal health and an understanding of the challenges facing livestock health as a part of a sustainable Agri-Food sector are desirable, as is experience of presenting and publishing. AU is a Bilingual Institution which complies with the Welsh Language Standards and is committed to Equal Opportunities. Students are welcome to apply in Welsh or English and any application submitted will be treated equally.

Stipend (Salary):

FoodBioSystems DTP students receive an annual tax free stipend (salary) that is paid in instalments throughout the year. For 2023/24 this is £18,622 and it will increase slightly each year at rate set by UKRI.

Equality Diversity and Inclusion:

The FoodBioSystems DTP is committed to equality, diversity and inclusion (EDI), to building a doctoral researcher(DR) and staff body that reflects the diversity of society, and to encourage applications from under-represented and disadvantaged groups. Our actions to promote diversity and inclusion are detailed on the [FoodBioSystems DTP website](#).

In accordance with UKRI guidelines, our studentships are offered on a part time basis in addition to full time registration. The minimum registration is 50% FT and the studentship end date will be extended to reflect the part-time registration.

References:

- Kleinhenz MD, Weeder M, Montgomery S, Martin M, Curtis A, Magnin G, Lin, Z, Griffin J and Coetzee JF (2022) Short term feeding of industrial hemp with a high cannabidiol acid (CBDA) content increases lying behavior and reduces biomarkers of stress and inflammation in Holstein steers. *Scientific Reports*. 12: 3683.
- Kliem, KE., Humphries, DJ., Jackson, KG (2023) Effect of lactation state on the ex vivo cytokine response of whole blood from lactating dairy cows. *Proceedings of the British Society of Animal Science Annual Conference 2023*, 14:417-418.
- Muthumalage T and Rahman I (2019) Cannabidiol differentially regulates basal and LPS-induced inflammatory responses in macrophages, lung epithelial cells, and fibroblasts. *Toxicology and Applied Pharmacology*. 382: 114713.
- Wonfor R, Natoli M, Rose M and Nash D (2017) Effects of preimplantation factor on interleukin-6 and prostaglandin F₂ α and E₂ on bovine endometrium. *Theriogenology*.102: 174-182.

For up to date information on funding eligibility, studentship rates and part time registration, please visit the [FoodBioSystems website](#).