Institution: University of Aberdeen

Unit of Assessment: 5 - Biological Sciences

Title of case study: Yeast as a feed additive that improves health and productivity in ruminants

1. Summary of the impact

When Rowett Research Institute (now Rowett Institute of Nutrition and Health, University of Aberdeen; RINH) scientists discovered that yeast, when used as a feed additive in ruminants, protected vulnerable, anaerobic microorganisms in the rumen from oxygen toxicity, the finding made sense of a range of disparate observations made previously by RINH scientists and others. The removal of oxygen leads to a cascade of benefits to ruminal fibre digestion, lactate metabolism and bacterial growth efficiency, which in turn benefits animal health and productivity. This seminal discovery transformed confidence among the livestock industry in the benefits of yeast as a feed additive. The use of live yeast in ruminant livestock production increased enormously as a result, such that the great majority of cattle in North America, and millions of cattle in Europe, now receive yeast routinely as a feed additive. Productivity has increased significantly as a consequence. *Claimed impacts have therefore been on animal health, husbandry, animal production yields, and hence on the economy, commerce and industry.*

2. Underpinning research

Before this discovery was made, a number of yeast, fungal and bacterial products had been suggested to have beneficial effects if provided as a feed additive to ruminants, with relatively little good evidence to underpin their use. Little if any mechanistic information was available. A DTI-LINK consortium consisting of 15 industrial companies and RINH was set up to investigate these claims. The work of this consortium and subsequent research contracts on this topic took place from 1990-1998 [1,3,4], with intermittent projects being undertaken up to and including 2012.

Yeast culture contains live yeast cells and residues of growth medium. In research undertaken at RINH, Wallace established that yeast culture stimulated the growth of ruminal cellulolytic bacteria, which are critical for optimal digestion of feeds, in the mixed rumen microbial community. The additive also lessened the incidence of acidosis, by rendering the mixed ruminal community less prone to lactic acid production, and increased the proportion of viable bacteria that could be recovered from the rumen (both shown first by the RINH team). However, the underlying mechanism was not understood, particularly how two apparently unrelated processes, carried out by different species of microorganism, benefitted from yeast supplementation. As a consequence, the feed industry and livestock producers generally had little faith in such products.

Several avenues were investigated by the Rowett research group led by Dr John Wallace (Principal Scientific Officer), supported by Dr Jamie Newbold as Senior Scientific Officer (now Director of Research at IBERS, Aberystwyth University) and Dr Ian Edwards, lecturer at the University of Aberdeen (retired in 2008). The discovery that provided incontrovertible evidence of yeast's mode of action was made in a series of experiments in which oxygen contamination in the rumen was the focus. Pure culture experiments showed that *Fibrobacter succinogenes* (the main cellulose digester) grew more quickly on cellulose when yeast was present. When traces of air were introduced into the growth tube, the growth inhibition which normally occurred was prevented by yeast. Twenty-one day incubations with ruminal digesta *in vitro* demonstrated once again the protective effect of yeast when air was introduced in small concentrations. Similar observations were made with ruminally cannulated sheep [1,2]. The most convincing evidence was provided when different strains of yeast and different cultivation conditions were compared: the benefit of the yeast was proportional to its respiratory activity. Strains with low O_2-scavenging activity stimulated the fermentation far less than those with high respiratory activity. Furthermore, when respiration-defective mutants of one of the latter strains were tested, they lacked any stimulatory activity in pure cultures or in the mixed rumen.

The multiple effects of the yeast on ruminal fermentation could now be seen as a cascade of events, flowing from the crucial protection of vulnerable bacteria, including both cellulolytic bacteria and lactate utilisers.

A period followed when the original observations were amplified and examples were provided. It emerged that the response to yeast was diet-dependent. In general, animals receiving diets that contained fresh forage responded less than animals receiving winter rations. The RINH team provided an explanation by comparing the oxygen-consuming activities of different materials It emerged that grass has among the highest oxygen-consuming activities in nature. Thus, freshly consumed grass retains mitochondrial activity, which in turn detoxifies oxygen and effectively protects ruminal microorganisms – an evolutionary adaptation that works well. Conserved diets contain grains and silage with low respiratory activity, however. These are the dietary conditions where yeast is most effective.

Two papers were published on the central discovery, leading to an acceptance by the scientific community [3, 4]. The main work of dissemination was focussed on the feed and livestock industries, via popular/trade articles and seminars/industry presentations. Many articles appeared in national newspapers and in trade journals such as *Farmers Weekly* and *Feed Compounder.* Proceedings papers from presentations at international trade conferences in the UK, France, USA, Mexico, Japan, Korea, China, Australia and New Zealand were distributed by companies such as Alltech, Lallemand and Lesaffre. The dissemination continues to the present day, the latest technical trade article appearing in *All about feed,* a Reed International publication, in March 2013. More scientific papers followed on from the original discovery, and invitations were received frequently to speak at animal science/nutrition meetings. As a result, acceptance of yeast increased rapidly. Other microbial additives fared less well: they lacked the oxygen-consuming abilities of yeast.

Work on yeast has continued at the RINH. Throughout the years, until the present, at least a dozen postgraduate students and visiting workers have contributed to the research. Its effectiveness in combination with other additives has been elucidated, and the effects on the microbial community demonstrated. The latest example is a 2012 SPARK grant from the Technology Strategy Board, which was awarded to investigate the applicability of FLOW-FISH to community profile in beef cattle receiving yeast. This small project enhanced once again RINH/ Aberdeen University involvement with practical livestock production, namely NE Scotland beef farmers. Invitations to speak about yeast at international conferences continue to be received, and, partly as a consequence of the yeast work, John Wallace was appointed in 2012 to the FEEDAP panel of EFSA, the European regulatory authority on the safety of foods and feeds.

3. References to the research

Refereed papers

[1] Newbold, CJ, R.J. Wallace, X.B. Chen, and F.M. McIntosh. (1995). Different strains of *Saccharomyces cerevisiae* differ in their effects on ruminal bacterial numbers *in vitro* and in sheep. J. Anim. Sci. 73:1811-1818. *This paper provided a corollary to the BJN paper below: the efficacy was strain-dependent and corresponded to respiratory activity.*

[2] Elhassan, SM, CJ Newbold, IE Edwards, JH Topps, and RJ Wallace. (1996). Effect of yeast culture on rumen fermentation, microbial protein flow from the rumen and live-weight gain in bulls given high cereal diets. *Anim. Sci*. 62:43-48. *This paper provided in vivo evidence of the in vitro observations.*

[3] Newbold, CJ, RJ Wallace, and FM McIntosh. (1996). Mode of action of the yeast *Saccharomyces cerevisia*e as a feed additive for ruminants. *Br. J. Nutr*. 76**:**249-261*. The seminal paper that revealed the way in which yeast protected ruminal microorganisms from oxygen toxicity*.

[4] Newbold, CJ, FM McIntosh, and RJ Wallace. (1998). Changes in the microbial population of a rumen-simulating fermenter in response to yeast culture. *Can. J. Anim. Sci*. 78:241-244*. In vitro demonstration of the cascade effect mentioned above.*

[5] Wallace, R.J, D Colombatto, and PH Robinson. (2007). Enzymes, direct-fed microbials and plant extracts in ruminant nutrition. *Anim. Feed Sci. Technol.* 145, 1-4. *The editorial introduction to a special issue that RINH staff co-edited, and contributed several original papers. Yeast is the archetypal 'direct-fed microbial'.*

Popular press, technical

[6] Wallace, RJ (1996) The mode of action of yeast culture in modifying rumen fermentation. In: Lyons, T.P. and Jacques, K.A. (Eds) *Biotechnology in the Feed Industry*, pp.217-232. Nottingham, UK: Nottingham University Press. *One of many popular articles disseminating to the industry.*

Grant support

1989-93 Department of Trade & Industry, £720,000. `Efficacy and mode of action of probiotics'. (with 8 others)
1995-98 Joint Studentship with the International Livestock Research Institute (el Hassan)
1997 Monsanto Feed additives £132,000
2001 EC Fifth Framework Programme QLK5-CT-2001-00992 'Rumen-up' 2,551,000 euros (coordinator)
2003 Marie-Curie Fellowship to Karola Glaeser, €114,072
2012 SPARK Technology Strategy Board, £5,000

PLUS annual core support £250-569K from the Scottish Government

4. Details of the impact

The knowledge that yeast culture protected vulnerable animals from oxygen contamination of their ruminal fermentation led to a rapid increase in acceptance of yeast culture by the feed industry and farmers [d]. Benefits to health and productivity of cattle were observed across the globe. Sales over sustained periods of time reflect whether farmers observe benefits. Precise data on sales are protected, however, it is known that yeast is supplied to the majority of feedlot cattle in North America, and in the UK perhaps one-third of cattle receive yeast culture (particularly during winter months when its benefits are most evident). One company, Alltech Inc., has grown from a $10M annual turnover in 1990 to in excess of $200M today, substantially on the back of yeast sales. Other companies that feature yeast as their headline product have expanded too; they include Lallemand, Diamond V, Biosaf and Lesaffre [a]. The last company's marketing depends entirely on spin-offs from original observations made at Aberdeen. The Lallemand product is marketed as the product LEVUCELL® SC as a specific live yeast *Saccharomyces cerevisiae* CNCM I-1077 preparation that enhances rumen efficiency. The product information states that… *"A feeding program using Lallemand products will have a positive effect on your livestock business".* See http://www.lallemandanimalnutrition.com/our-products/ruminants/. The 'increased rumen efficiency' arises from the oxygen-protective effect.' Another example, indicating the scale of use in North America, can be found at http://www.rumenco.co.uk/product/19/Diamond-V-XP-Yeast.html. [c].

A recent meta-analysis (Poppy et al., 2012, J. Dairy Sci. 95, 6027) indicated that the benefit of yeast was an increased milk production of 1.16 kg/cow/day, or 423 kg/cow/yr. The farm gate price of milk is £0.31 per kg (http://www.dairyco.org.uk/market-information/supply-production/milk-production/uk-monthly-and-annual-milk-deliveries/), so the benefit per cow would be £ 0.31 × 423 = 131/cow/year. The dairy herd comprises 1.81M cows (http://www.dairyco.org.uk/market-information/farming-data/cow-numbers/uk-cow-numbers/). A conservative estimate would be that one-third of all UK dairy cows receive yeast, therefore the total UK benefit from feeding yeast to dairy cows would be £M 131 × 1.81/3 = £79M per annum. As the beef industry nationwide has a value of £2.42bn (EBLEX, http://www.eblex.org.uk/wp/wp-content/uploads/2013/05/p_cp_eblex_balancing_the_market_final_220512.pdf),and the percentage response in beef animals to yeast is greater than dairy, the total benefit from yeast must exceed £110M per annum in the UK cattle industry.

The impact of the research continues as the yeast market continues to grow. The Ruminant Product Development Manager of AB Vista, formerly of Lallemand, provided an analysis indicating that sales of yeast in the feed industry globally were worth around £196M in 2009, growing to £214M in 2013 [b]. She indicated major opportunities for expansion in Eastern European and Asian countries.

Part of the impact of the research was consultancy work generated as a result of the discoveries, benefitting both the companies and the University. The livestock industry is one that is acutely aware of efficacy. If a product has no benefit, farmers won't use it. The vast sales show that it does work and farmers' confidence is enhanced, partly by the Aberdeen research results, which the feed companies transmit to them as 'how yeast works'. Confidential research contracts were awarded through the then commercial arm of RINH, Rowett Research Services, throughout the 1990s and 2000s with the major companies involved in yeast, including Alltech, Lallemand, DCL Yeast Ltd, Biosaf, Lesaffre and Sanofi.

Therefore, research that catalysed the impact that has been manifest within the REF window has its origins in the 1990's and continues to this date. The discovery of the mode of action of yeast in the rumen led directly to two contributions to legislation and contributed to a deep involvement in another. Wallace was called to Brussels in 1999 to advise the European Commission's Scientific Commission on Animal Nutrition (SCAN) in drawing up their registration requirements to control feed additives: in particular, SCAN needed to understand our findings that metabolically active, but not necessarily live or growing yeast, can effect the benefits to ruminal fermentation. The second direct involvement was that Wallace wrote the mode of action section of the dossier submitted by Alltech to SCAN in the late 1990s. The influence of Wallace's work on yeast, among other feed additives, resulted in his appointment in 2012 to FEEDAP, the successor to SCAN in the European Food Safety Authority (EFSA), possibly the greatest impact stemming from the original research. This research continues to have policy relevance because, under Article 10.2 of Regulation 1813/2003, all feed additives already approved and on the market must be re-authorised. Evidence of the mechanism of action of yeast as an animal food growth enhancer and the experience gained from the research therefore have high relevance to current EFSA policy decisions.

Claimed impact as defined by REF guidance:
Thus the impact generated as defined by REF includes*: impact on public policy, legislation and and services. The team was also engaged by leading companies to advise on dossiers to be submitted for regulatory approval, thus having an impact on commerce in the area of gain in productivity and reduction in costs of food. Demonstrable collaborations with industry have occurred and commercial adaptation of a new process concept and in husbandry methods has occurred. The research affected animal health and production yields of livestock. Gains in productivity have been realised as a result of research-led changes in practice.*

5. Sources to corroborate the impact

As well as the above, examples are given in attached testimonials and corroboration of specific claims made in this case study have been provided by the following senior industry experts:-

[a] Ruminant Research and Development Manager, Lesaffre
"*Certainly the results of research by Wallace and Newbold have been instrumental in giving the livestock industry confidence in yeast products, including our own."*

[b] Ruminant Product Development Manager, AB Agri (part of AB Vista), Marlborough, UK.
"The papers published by the Wallace group in the mid-90s ... marked a turning point in the exploitation of yeast as a feed additive".

[c] President & Chief Science Officer, Sage Biosciences, Canada.
"*Without your and your colleagues' efforts and findings, I doubt whether the industry would have developed to its current level of sophistication"*

[d] Ruminant Research and Development Director, Cargill Animal Nutrition, Belgium.
"*Dr Wallace and his colleagues played a key role in understanding the mode of action of live yeast ... This research achievement has had a significant and lasting impact on ruminant animal production".*