COMMERCIAL CONSIDERATIONS IN THE DEVELOPMENT OF TRANSGENIC CROPS AND AGROCHEMICALS FOR CROP PROTECTION

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ABSTRACT

The introduction of genetic approaches to pest and disease control raises many complex questions:

Can agrochemicals be replaced by genes? Can chemical solutions be replaced by genetic solutions? Will genetic control of pests and disease be more long lived (durable or sustainable) than the chemical approach? How can genetic and chemical approaches be handled in integrated programmes to realise the best of both worlds? Will increasing crop value lead to increased demand for "perfect crop protection"?

We address these issues, particularly in relation to fungal and insect control, but anticipate generating more questions than answers. At present, it is possible to speculate and to generate a wide range of scenarios, what is clear is that knowledge of how to integrate the widening range of options will be essential for future success.

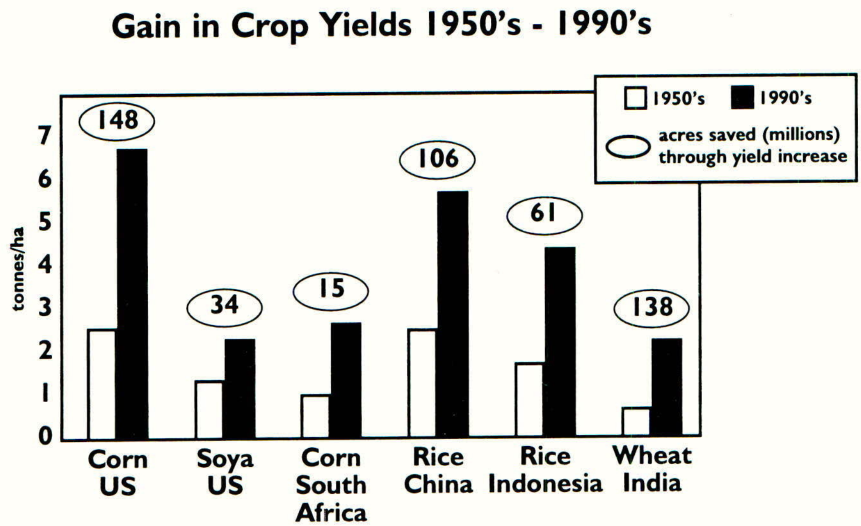
INTRODUCTION

Agrochemicals have been established for more than fifty years, the advantages and disadvantages of their use in crop protection are well known. Before agrochemicals were available for crop protection the only methods available to the grower were "biological control" through crop rotation and the use of resistant varieties. Over the last half-century, the combination of improvements in agronomy, fertiliser use, crop genetics and agrochemicals has enabled increases in crop yields to keep pace with the growth in population and the increased demands for high quality food supplies at an ever decreasing unit cost.

- Can agrochemicals be replaced by genes? Can chemical solutions be replaced by genetic solutions?
- Will genetic control of pests and disease be more long lived (durable or sustainable) than the chemical approach?
- How can genetic and chemical approaches be handled in integrated programmes to realise the best of both worlds?

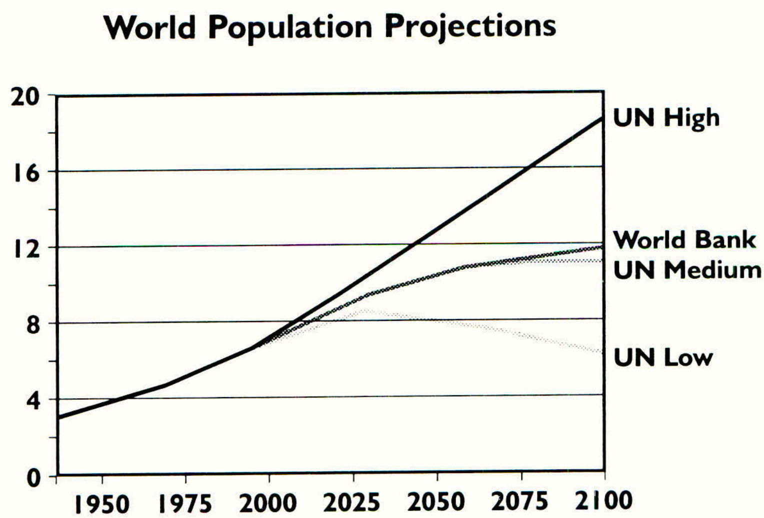
• Will increasing crop value lead to increased demand for "perfect crop protection"?

We address these issues, particularly in relation to fungal and insect control, but anticipate generating more questions than answers. Perhaps this is going to be the hallmark of the future which we would anticipate as Knowledge-Managed Agriculture.



From D T Avery (computed from FAO Annual Production Yearbooks)

Future population growth is still predicted and the benefits of traditional approaches to crop husbandry may be reaching practical limits. The introduction of transgenic routes to pest , disease and weed control opens up new opportunities to maintain the rate of increase in harvested yield.



THE AGROCHEMICAL ADVANTAGE

Agrochemical control of pests and diseases commenced historically with protective treatments which had to be applied frequently and at high dose rates. An example is copper or sulphur for control of fungal diseases in vines. These approaches worked and gave the grower the option of preserving the crop from disease but if disease was already present no curative effect was obtained . Many so called multiple mode of action fungicides were developed, but it was the advent of the curative systemic triazole fungicides which opened up major disease control strategies for crop protection. The protection of the flag leaf of cereals combined with fertiliser and higher yielding varieties gave rise to the "ten ton" clubs of highly productive, intensive farmers.

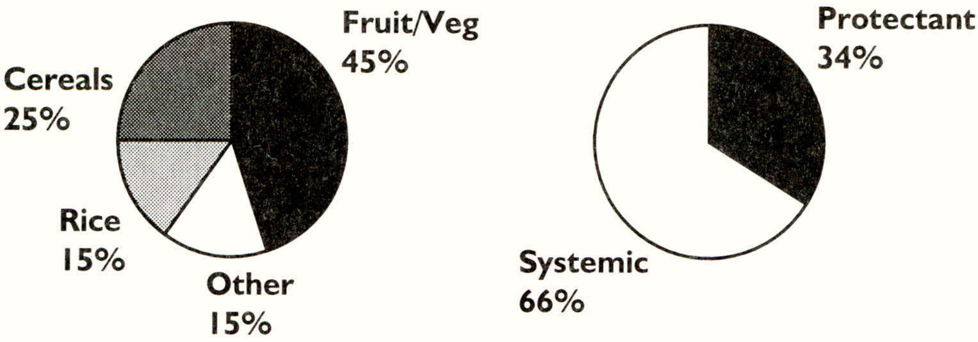
Modern fungicides, such as Azoxystrobin give safe and effective disease control of a range of diseases in many crops.

Insect control follows a similar trend. Before modern insecticides were developed only crude and highly toxic plant extracts were available for control of insects. The development of chemicals progressed over decades to give the pyrethroid insecticides such as "Karate" which give effective and broad spectrum control of a variety of insect pests. Such products can be used to eradicate invading insects at a point when the pest reaches an economic threshold, hence sophisticated scouting techniques can be used in crops such as cotton to determine the optimum time for spraying.

World Fungicide Market (1995)

Total value at end-user level = $6 billion

Source: Wood Mackenzie



Fungicides: by crop **Fungicides: properties**

Generalising from these examples, we can see that agrochemicals have six key advantages (Table 1).

Table 1. The agchem advantage

- KNOWN: Properties understood and accepted by farmers
- AS NEEDED: Only used when economic return justifies use
- CURATIVE: Eradicant effects against a broad spectrum of pathogens/ pests
- RANGE: Effective on many crops at the time of need
- TIMING: Used at a variety of times in the crop growth cycle
- MIXTURES: Used in mixtures to control a range of diseases and prevent resistance

NEW GENES FOR OLD PROBLEMS

Control of Pathogens

Classical plant breeding has invested heavily in screening germplasm for disease and pest susceptibility. For instance CIMMYT estimate 60% of their current effort is devoted to this area (Braun *et al,* 1998). Sophisticated breeding approaches to introgress new sources of resistance have been used over many years to give effective baseline control of fungal diseases and the variety classification and listing procedures in EU and US give prominence to this aspect. Thus, in wheat many genes giving resistance or susceptibility to races of *Erisyphe graminis* are known and used by breeders to create a background level of resistance as new fungal races emerge and the old resistance genes are overcome. Nevertheless, in intensive agricultural systems such as in the EU, economic benefit from fungicide treatments are large, and this market is currently worth $6 Billion /pa.

In contrast, the presence of new, classically bred resistance genes in varieties has not attracted a premium. Neither is there any well documented information as to how different disease control strategies fit with the different genetic backgrounds in the economic equation

One of the goals of biotechnology research is to develop varieties with more complete and durable resistance to disease. The research on fundamental aspects of how plants and pathogens interact and the genetic basis of the classical resistance genes is now coming to fruition, so rapid progress on the science is certain. What will this mean for the commercial arena, and how will it exemplify the advantages of gene-based control?

- Protective effects from introduced genes have been delivered. (see Melchers & Stuiver, this volume) A variety of genes have been used, chitinase, glucanase, pathogenesis related proteins (PR proteins) and a series of anti-fungal proteins (AFP). These single or combined genes do not give complete immunity and are pathogen specific. (Collinge *et al.*,1994; Broglie and Broglie, 1993; van den Elzen *et al.*,1993; De Bolle *et al* 1995).
- Broader spectrum pathogen control can confidently be anticipated. For instance, genes such as *mlo* (Buesches *et al,* 1997) involved in the signal transduction from a number of race-specific interactions are now being identified. Multiple genes will also allow the potential for broader spectrum control.
- Chemical induction of disease response genes has been demonstrated to deliver at least partial resistance to disease. Interestingly, the type of disease control achieved is very different to the expectation in the farming community. Resistance is expressed after a delay of many weeks from the treatment, some education is needed to explain the biological results (Ruess *et al,* 1995)

Control of Insects

Commercial development of transgenic insect resistance is further developed thanks to the knowledge of the toxin produced by *Bacillus thuringiensis (Bt).* The bacterium has been used in biological control for more than fifty years. In 1983 it was suggested by Barton and Brill that the toxin gene from the bacterium could be transferred to a plant to give control of insects. It took fifteen years for this to become a commercial reality. Bt expressed in cotton has achieved considerable success and illustrates the potential of genetic routes to insect control, especially when narrow spectrum control is required. Although many companies are interested in achieving pest control by using related genes, there are few public announcements of success. We must assume that any new genes which code for proteins giving such highly effective insect control are valuable and that such genes must be wisely used. This has been recognised in the regulatory clearances for Bt-containing plants with the requirement for resistance monitoring and refugia . Bt is used to control pests of cotton, corn and potato. Each gene gives specific control of a narrow range of pests. Multiple genes will be needed for broad spectrum control.

Other genes have been identified, cloned and expressed in various plant tissues. These include, protease inhibitors, alpha-amylase inhibitors and lectins (Boulter,1993; Shi *et al., 1994;* Gatehouse *et al,* 1992). Each of these classes of protein has activity against specific insects or groups of insect, however, many problems remain to be overcome, some of the proteins are too specific, some have only marginal activity, requiring very high expression of the protein in the recombinant plant tissue, some have significant toxicity to mammals. There is no doubt however that the search for novel insect toxins is continuing, we expect interesting and novel discoveries to be made in the next decade.

From the current state of gene-based control, we can pick out the five key advantages of gene-based crop protection to contrast with those for chemicals.(Table 2).

Table 2. Five gene benefits

- PROTECTIVE: The gene effect is active on first attack so targets the earliest stages of pest or disease development
- THRESHOLD: The economic threshold for use is lower in that treatment cost is essentially zero unless a switched trait is used; this can convert uneconomic chemical opportunities (cryptic losses) into valuable benefits. The fact that no manufacture of a chemical is required reduces the capital investment needed to launch a product.
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- SPECIFIC: Single major effects can be targeted with little impact on other species
- ACCESS: The gene product can be produced in plant parts difficult to reach with chemical treatments because of timing issues (late season) or physical restriction such as roots.
- NO RESIDUE: The considerations of residues and exposure do not disappear completely, but opportunities exist, (e.g. post-harvest) where chemical residue considerations limit their use

SHAPING THE FUTURE MARKET

While many options appear to be opening up there are still many constraints placed upon the farmer or grower. The value of crop protection is normally expressed as approximately 25% of the value of the crop when sold to the processor. Even with perfect disease or pest control , this value is unlikely to increase. The grower will be presented with a wider range of choices. Estimation of the efficiency of the treatment,
the cost, fit with customer requirements and the flexibility to adapt to change in climate, pest or disease will remain as difficult as ever.

The use of Karate insecticide in cotton crops expressing Bt clearly demonstrates the advantages of each approach being combined to give broad spectrum and cost-effective control while also reducing the opportunity for resistance to develop.

Plant biotechnology will have an impact on crop value, as new properties are added to plants to give specific end user attributes. The value of protection will, therefore, also increase. The introduction of genes for crop protection can have the opposite effect of reducing the value of crop protection applied as a chemical treatment as different ways of achieving the effect compete in the market..

Our analysis suggests that both chemical and gene effects will be used for the foreseeable future specialising increasingly in areas of key strengths. As a consequence, the knowledge-intensive farming of the future will develop sophisticated integrated crop treatment systems to maximise benefits from both. The use of chemical switches to link the benefits of chemical flexibility to gene effects is an aspect of integrated control which we find particularly intriguing (ref)

The key unresolved question is the future division of the value for crop protection among the different treatment regimes which are required to give the farmer assurance that the crop will survive until harvest and retain the value in which he has invested. It is clear that the major agrochemical companies are divided on this answer as judged by their investment strategies.

The future must be about investment in knowledge - intensive agriculture. The decisions required about crop protection will be complex and will depend on a variety of forecasts and on information to apply to the field situation in an integrated way. The development of this knowledge base will be critical to all those involved in support of agriculture.

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