## K.P. PARRY

Herbicide use and invention

This chapter will deal with herbicide use and invention. The first part will cover the background of the agrochemical industry, i.e. the 'use' side, and in the second part an outline of herbicide discovery will be given.

Background to agrochemical industry

'Why use herbicides?' There are three prime reasons for using herbicides: to increase yield of a crop by reducing competition for light and water from other species (weeds); to improve crop management -- particularly harvesting, raising the quality of the final harvested crop/seeds, fruits; to reduce the risk of cross-infection from fungi and insects, from weeds to the crop.

Some idea of the effects of specific weed infestations of maize on yield can be seen in Figure 1 (Aldrich, Scott & Long, 1975). The data show that failure to control weeds, particularly early on in the growing season, can lead to losses of up to 20%.

Fig. 1. Yield. (Bu = Bushels)

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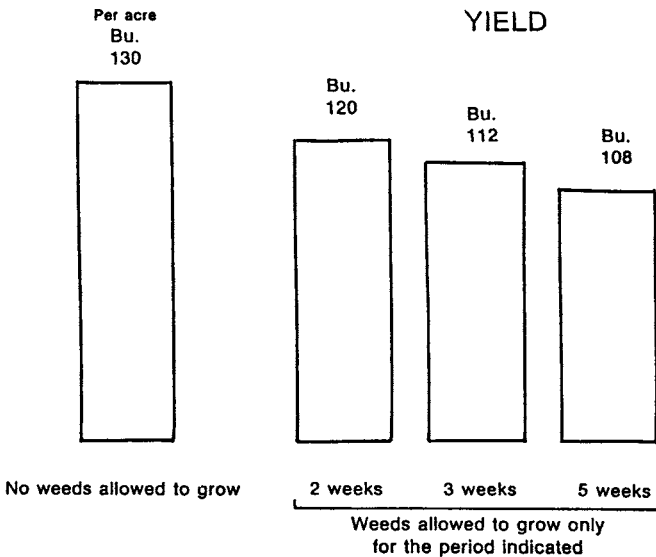
Other data from the US, in soya, indicate similar effects (Figure 2) (Walker *et al.*, 1984; Shurtleff & Coble, 1985). In both cases, yields were deleteriously affected by increasing infestation either in total or over time.

In the UK, infestation in cereals occurs with both grass weeds, e.g. *Alopecurus myosuroides*, and broad-leaved weeds like charlock. Again the effects on yield of a treatment particularly early in the season can have dramatic effects, particularly so in the case of the grass (Figure 3) (Wilson, Thornton & Lutman, 1985).

There are different advantages in controlling broad-leaf weeds or grasses. If control of *Alopecurus myosuroides* was delayed, yields declined more rapidly than by delaying the control of broad-leaved weeds (see Figure 3). In the early stages of competition there is a tendency for the broad-leaved weeds (*Galium aparine*) to increase the total dry weight of the biomass whilst the grass *Alopecurus myosuroides* replaces the crop (Wilson, Thornton & Lutman, 1985). At harvest, weights of material other than grain were similar, irrespective of treatment, weeds, etc but large differences in grain yield arose. The cost efficiency of combine harvesting is therefore much impaired (Figure 4) (Elliott, 1981).

Overall effects on harvesting are difficult to quantify as they depend to a considerable extent on the nature of the combine harvester used and its method of
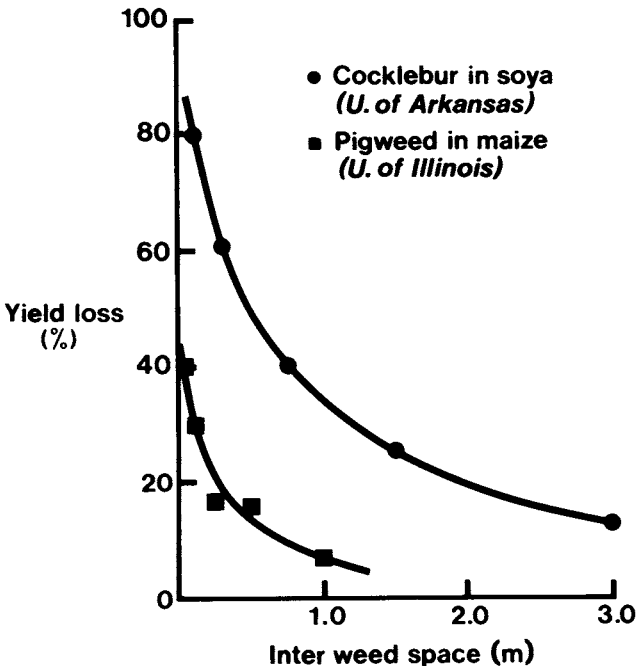
Fig. 2. Effect of season-long weeds on yield.

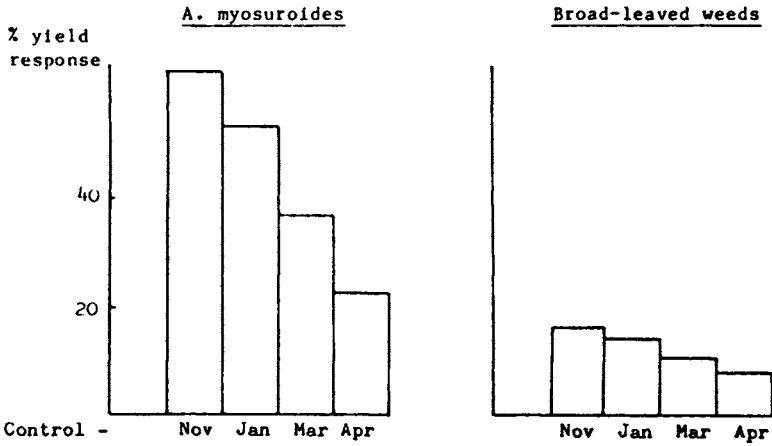Fig. 3. Effect of delaying control on mean % yield response (excluding Newington).

Fig. 4. Stem and dry weight assessments in early May at Merriscourt (*A. m = A. myosuroides*).

| Timing of Control A.m.	Dicots	Barley Stems/plant	Dry wt g/m²			
			Barley	A. myosuroides	Dicots	Total
Nov.	Nov.	4.7	1145	0	0	1145
Nov.	Jan.	4.7	1020	0	0	1020
Nov.	Mar.	4.5	938	0	14	952
Nov.	Apr.	4.7	1083	0	50	1133
Nov.	None	4.9	1013	0	64	1077
Jan.	Nov.	4.5	892	7	0	899
Mar.	Nov.	3.7	785	135	0	920
Apr.	Nov.	3.8	685	330	0	1015
None	Nov.	3.8	687	354	0	1041
None	None	3.5	547	491	18	1056
S.E. ±		0.25	64.3			60.3

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operation. Elliott (Elliott, 1981) has attempted to quantify the effects and some of his results have been used in Figure 5 (MOG = material other than grain).

World market sizes

Figure 6 shows the growth of the agrochemical market over the last few years. There has been a particularly large expansion from 1970–80 with a slight reduction in growth in recent years (Wood, Mackenzie & Co, 1981–6). It is interesting to note the slight fall in 1983 – attributed to the PIK (Payment in Kind) programme in the USA where the government legislated to effect a reduction in land usage. The agrochemical market appears to have recovered so limitations on land use about to be introduced in the EEC and USA may not have a serious long-term effect. The herbicide market has grown in a very similar fashion to the total market and now constitutes about 40% of the total. Insecticides make up another 40% whilst the balance is fungicides.

Markets for herbicides fall into two major classes: selective and non-selective. In the former, weed control in a major world crop, e.g. maize, soya, cereals, rice is the prime objective whilst, in the latter, the paraquat and glyphosate market, total vegetative control is desired. Some idea of individual markets is given in Figure 7 showing the value of particular herbicides used in crops. Thus the total market for herbicides used in maize for a wide variety of uses is in excess of $1000m. A different

Fig. 5. Cost of processing MOG put at £10/t. Grain selling price roughly £80–100/t.
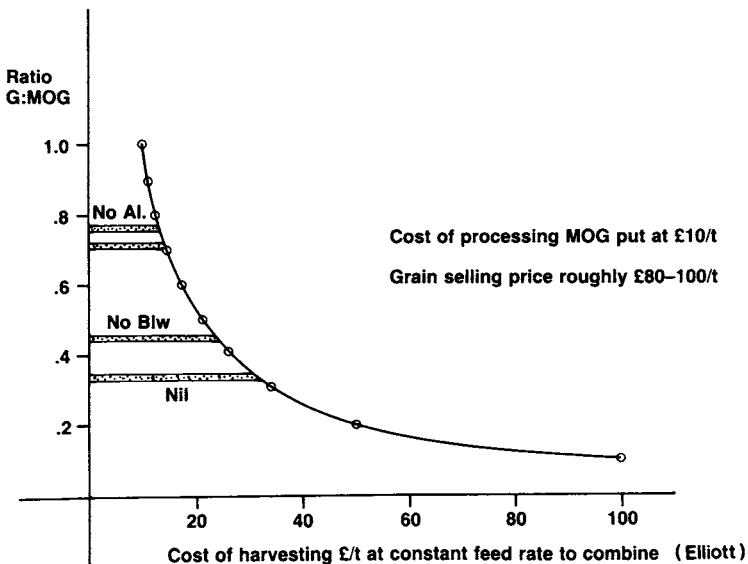
segment of the selective herbicide market is a herbicide which kills a particular range of weeds, e.g. a grass killer or graminicide approximately $2000m. The market for total vegetative control, the paraquat and glyphosate market, is believed to be somewhere about $800m.

Market structure of products

A considerable range and number of products are now available. Figure 8 shows the number of products available in the UK over time. A significant increase in

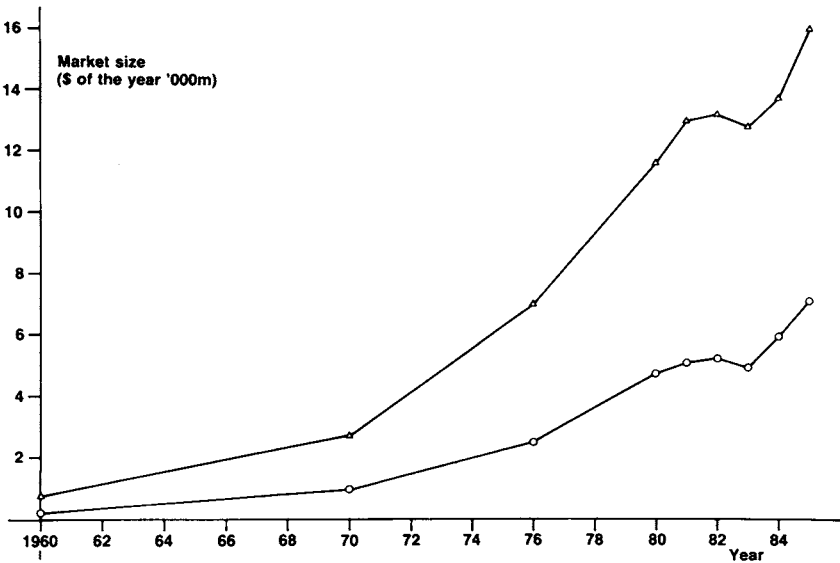Fig. 6. Agrochemical market size with time.

Fig. 7. Herbicide usage per crop sector (end user).

	1979	1985
Maize herbicides	1050 M$	1575 M$
Soya herbicides	760 M$	1475 M$
Cotton herbicides	350 M$	340 M$
Graminicides	1930 M$ (1982)	
Total Vegetative Control	>800 M$ (1982)	

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the late 60s and early 70s is followed by a plateau (Corbett, 1979; Hill, 1982), with a total of 561 products now available (Makepeace, 1986).

If current chemicals are classified in terms of a chemical toxophore, some interesting observations are apparent. First there are a smallish number of toxophores which have produced a large number of products. For instance, Figure 9 illustrates some very common herbicide structural types and Figure 10 the number of products which have come from each of these groups (Wood, Mackenzie & Co, 1981–6). Some idea of the size of production can be gained from Figure 11.

Figure 12 shows that some 50% of herbicides are single compound toxophores and a remaining 30% arise from those groups already illustrated (Figures 9 and 10).

Another interesting feature is to look at the growth rates of these different groups of herbicides, Figure 13 (Wood, Mackenzie & Co). One very general observation is that the older herbicidal groups are least profitable. A product matures until it is displaced by a more cost-effective material in the technically advanced parts of the world. The developing countries will presumably continue to use the older commodity products for cost reasons although eventually the newer replacements will become commodity products and be used in these markets.

An examination of Figure 13 leads to the speculation that the hormones of 1945 are probably about to be displaced by Du Pont's sulphonylureas. We could speculate that the next set of compounds to disappear from the agrochemical scene would be triazines, carbamates and ureas. Replacements will need to be active at much lower rates and be safer environmentally.

Fig. 8. Approved products total (Crop protection approval scheme v. time). *Source*: Makepeace –Agricultural Chemicals Approvals Scheme ARC. WRO (Oxford).
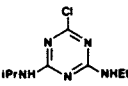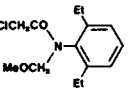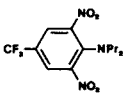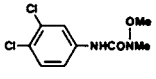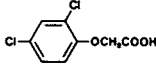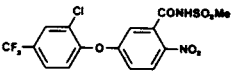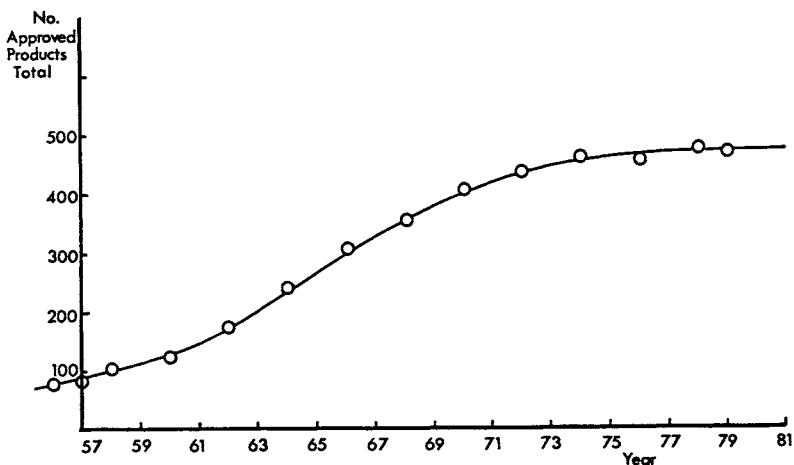
General trends within the industry seem to indicate that application rates are falling (Figure 14) (Graham-Bryce, 1981).

What is the lowest rate that could be used? A value of 2.5 x 10^{-6} g/ha has been estimated assuming one molecule of herbicide is required per cell of living tissue to effect death (Corbett, Wright & Baillie, 1984). Some of the assumptions are considered to be debatable by these authors and the figure possibly inaccurate by a factor of 10^3, but application rates of the order of mg/ha should be possible.

Another view is to examine the toxicological values for a number of well-known poisons, Figure 15 (Registry of Toxic Effects of Chemical Substances, 1976).

Fig. 9. Major herbicide types.

Generic Group	Est. Market Size ($m)	Typical member
Triazines	1425	Atrazine
Amides (haloacetanilides)	940	Alachlor
Carbamates	765	EPTC
Toluidines (dinitroanilines)	660	Treflan
Ureas	670	Linuron
Hormones	435	2.4.D
Diphenyl Ethers	345	Flex
Others	1835	includes paraquat, glyphosate, diazines etc.

Assuming a biomass at the time of spray of roughly 1–5 tonnes/ha, and a tox of 20–50 µg/kg, we could get application rates of about 20–250 mg/ha. Irrespective of method, it would appear that there is still scope for increasing activity levels.

Pesticide development

A general outline of the processes involved in developing a new pesticide is outlined in Figure 16.

Initially, exploratory testing in the glasshouse works synergistically with chemical synthesis. When active analogues have been selected, these are then tested on the field and given limited toxicological studies (simple studies of behaviour in soil and rats). Patenting is also initiated, and if the performance of a compound is good, further field testing, more toxicological studies and research for a manufacturing route are initiated. If the compound continues to show good activity and is cost effective, development will lead to marketing.

An idea of the timescale involved in development is shown in Figure 17 (Braunholtz, 1981).

Exploratory work at the early stages is the least expensive whilst later development and associated toxicological work makes major cash demands. The cash flow, illustrated in Figure 18 (Green, 1977) shows that there is a large financial outlay between years 4 and 6 and the product may not start to pay back until some ten years after discovery. A couple of points to note are that , although research is a fairly cheap

Fig. 10. Products and development compounds, arising from a particular toxophore.

Ureas	26 }	37
Alkoxyureas	11 }	
Carbamates	16 }	34
Thiocarbamates	19 }	
Triazines		29
Diphenylethers		29
Haloacetanilides		24
Dinitroanilines		22
Phenoxyacetics		17
Aryloxyphenoxys		17

Fig. 11. Estimated US production 1984.

thousand tons

Atrazine	**39**
Cyanazine	**13**
Diuron	**2–3**
2.4.D	**30**
Alachlor	**50**
Glyphosate	**12**

Fig. 12. Distribution of products/toxophore.
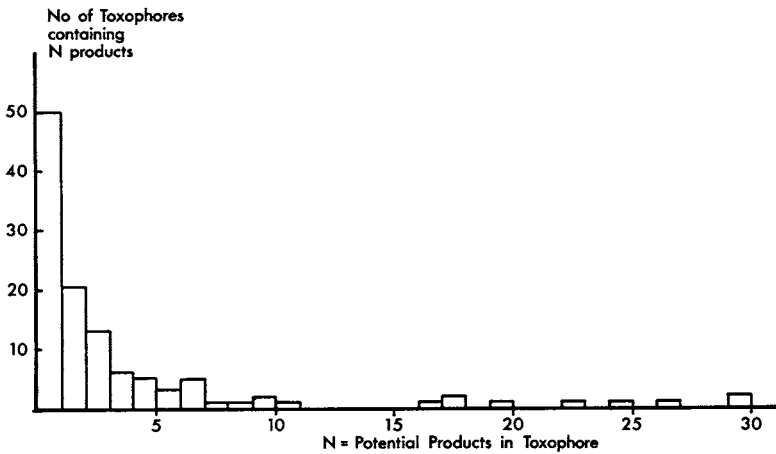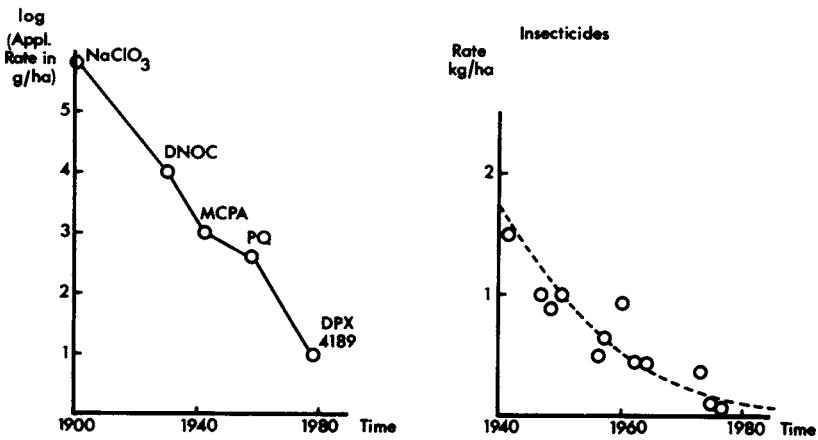

No of Toxophores containing N products

N = Potential Products in Toxophore

Fig. 13. % growth rate – herbicides.

	Year of introduction	1972–85 (real)	1985–90 (est)
Hormones	1945	0.2	−5.0
Triazines	1956	4.0	−3.1
Carbamates	1954–8	4.9	0
Ureas (inc. S.U.)	1960	1.7	5.2
Toluidines	1965	6.4	−2.0
Amides	1966	8.1	2.2
Diphenylethers	1970	19.2	9.3
Diazines	1974	19.1	5.4
Market		4.6	4.2

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Fig. 14. Application rates for representative crop protection chemicals v. time.

Source: Graham Bryce