Medical Research Council

Institute for Environment and Health

IEH assessment on

OILSEED RAPE: ALLERGENICITY AND IRRITANCY

1997 ASSESSMENT A3

Preface

Rape seed oil and its products are a valuable commercial resource for the UK. However, increasingly there have been concerns over possible health effects on those people who live close to areas where oilseed rape is intensively grown. Most of the concern arises over whether or not this plant emits biological or chemical substances to which people are especially allergic or sensitive.

To address these concerns a systematic review has been undertaken by the MRC Institute for Environment and Health (IEH) at the request of the Home-Grown Cereals Authority (HGCA) and the Ministry of Agriculture, Fisheries and Food (MAFF). This extensive review of the published literature, together with a workshop, has resulted in the first comprehensive assessment of the possible health effects of this crop.

As Chairman of the workshop I would like to acknowledge the contributions of staff at the MRC IEH who have provided the substance of this report and the HGCA, MAFF, the Department of the Environment and the Department of Health for their input to the discussion and their help in drawing together and evaluating the available evidence.

Workshop participants are listed at the end of this assesssment.

Stephen Holgate, Workshop Chairman

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Executive summary

BACKGROUND

The quantities of oilseed rape grown in the UK have increased considerably since the 1970s and, in recent years, there has been increasing concern over possible health effects among people living in close proximity to fields of oilseed rape. For this reason the Home-Grown Cereals Authority and the Ministry of Agriculture, Fisheries and Food requested the Institute for Environment and Health (IEH) to prepare a review on the allergenicity and irritancy of oilseed rape and to assess the possibility that adverse health effects might be associated with the crop.

REVIEW PROCESS

As a first stage in the review process IEH prepared critical reviews of the literature on crop production, the chemistry of oilseed rape, and pollen levels and transport, and on health effects reported to be associated with oilseed rape. Experts in crop production, pollen biology, veterinary medicine, allergy and clinical medicine were then invited to discuss the issues at a workshop held in Leicester in November 1996. The purpose of the workshop was to ensure that the IEH review was up-to-date, accurate, comprehensive and balanced, to make an expert assessment of the likely health effects associated with oilseed rape, to identify key gaps in knowledge and to make recommendations for further research.

HEALTH EFFECTS ASSESSMENT

Some, mainly atopic, individuals may have an allergic response to oilseed rape pollen. However, sensitisation to oilseed rape pollen alone appears to be rare, and the public health impact seems to be minimal in comparison with that of other pollen allergen sources. Furthermore, no causal association can be established, at this time, between exposure to oilseed rape and non-specific symptoms of general malaise.

There is currently no direct evidence to suggest that volatile organic compounds (VOCs) emitted by oilseed rape are responsible for any adverse health effects associated with the crop.

MAIN RESEARCH RECOMMENDATIONS

❐ Standardised oilseed rape pollen extracts should be developed for use in epidemiological and challenge studies.

❐ Volunteer studies should be carried out to determine whether levels of VOCs and/or fungal spores associated with oilseed rape can cause adverse health effects, and to investigate the incidence of monosensitisation to oilseed rape pollen and interactions between oilseed rape pollen and common air pollutants.

❐ Epidemiological studies should be undertaken to follow potentially susceptible groups throughout the oilseed rape season, monitoring symptoms in conjunction with environmental factors.

❐ The distribution of oilseed rape pollen in rural communities should be investigated in relation to other sources of pollen.

❐ The interactions of particles derived from oilseed rape pollen with other air pollutants should be investigated.

❐ The concentrations, relative proportions and dispersal of VOCs produced by oilseed rape should be studied.

1 Oilseed rape production in the UK and Europe

1.1 BRASSICA OILSEED SPECIES

There are four main species of *Brassica* cultivated for their oils world-wide. *Brassica napus* L. and *Brassica rapa* L., (syn. *campestris* L.) are the two rapeseed species grown in Europe and the UK. *Brassica juncea* Czern. and Coss. (brown mustard) and *Brassica carinata* Braun (Ethiopian mustard), which are not grown in the UK or Europe, tend to be cultivated in drier regions of the world. *B. napus*, more commonly known as (oilseed) rape, is the non-bulbing form of swede, and is probably the main *Brassica* oilseed species grown in Europe. *B. rapa*, a non-bulbing form of the true turnip, is more commonly known as turnip rape. Both winter (autumn sown) and spring varieties are grown as a source of seed which is crushed for oil. The yield from the autumn sown varieties is generally highest, as long as conditions are favourable. Winter varieties generally predominate in Europe. Varieties of *B. rapa* are probably the most cold-hardy (Kimber & McGregor, 1995; Pouzet, 1995).

A related species *Sinapis alba* L. (formerly *B. hirta* Moench), often known as white mustard, is commonly grown in Europe as a source of condiment (Kimber & McGregor, 1995). World-wide, *Brassica nigra* (L.) Koch. (black mustard) was grown along with *S. alba* but has now been largely replaced by *B. juncea* (Hemingway, 1995).

Many different varieties of rape are available. The variety selected for production is dictated by the prevailing environmental conditions, particularly climatic factors, as well as the intended market. Some varieties are particularly useful for the edible oil market, whilst others are more useful for industrial or pharmaceutical purposes (Pouzet, 1995).

Currently, 'double-low' varieties which have a very low erucic acid and glucosinolate content in the seed are required for the edible oil and animal feed market; high erucic acid rape (HEAR) varieties are available for specific industrial uses.

1.2 CROP DEVELOPMENT

Throughout most of Western Europe, milder winters allow the growth of winter varieties of rape, which are sown in late summer to early autumn. These winter varieties require a period of cold ('vernalisation') to flower without delay the following year. Plants sown before the winter can take advantage of a longer growing season, and so usually produce a higher yield than spring sown crops. Thus seed sown in late August-September develops to produce plants which flower in April/May of the following year and are harvested in July. Inflorescence initiation on large plants sown in August can occur as early as November. On smaller plants, however, this may not occur until the following spring (Mendham & Salisbury, 1995). Spring varieties predominate in more northern latitudes. In the UK, spring oilseed rape is sown in March/April and harvested in August/September.

B. napus is self-fertile (McCartney & Lacey, 1991), although both insects and wind can also play a role. Experiments have demonstrated that bees increase the number of ovules that are fertilised and the synchronisation of fertilisation throughout the crop. Therefore, beehives placed close to the crop should be of potential value in crops able to produce large numbers of seeds (Mendham & Salisbury, 1995). The potential honey yield from winter oilseed rape can be 50 kilograms/hectare. Flowering rape also provides an important food supply for native bumblebees (Marquad & Walker, 1995).

The *Brassica* oilseeds are harvested by combine harvester in the UK. In many cases the crop is directly combined after it has been left to senesce naturally or after a desiccant has been applied. These methods are used on about 65% of the UK crop. An alternative method is to cut the crop and to leave the cut stems and pods in swaths to ripen in the field before combining.

1.3 PRODUCTS OF OILSEED RAPE

There are a number of different uses for the oil extracted from rape. As well as oils and margarine for human consumption, there are a number of non-food industrial uses. After the oil has been extracted the remaining meal is high in nutritionally valuable protein. The fibre content of the plant, which is of low nutritional value to non-ruminants, is of particular interest to animal nutritionists (Uppström, 1995).

The chemical composition of the oil varies between varieties and fatty acid composition is of particular importance with respect to its final use. Oil derived from rape seed can provide an alternative to other fats in the diet. Dietary fat has a number of important nutritional functions in humans; it has, however, also been implicated in the aetiology of a number of chronic diseases including cardiovascular disease, cancer and hypertension. Double-low rape oils, which are also low in saturated fatty acids (<4% palmitic acid), with relatively high levels of oleic acid (55–60%) and linolenic acid (8–10%), are of great value as edible oils for human consumption, and have been shown to reduce plasma and low density lipoprotein cholesterol levels (McDonald, 1995).

Oils which have a high content of long chain fatty acids, particularly erucic and behenic acid, are used in industry to make a range of products from photographic materials to cosmetics (Sonntag, 1995). Owing to the finite nature of fossil fuels and the increased public awareness of air pollution, plant oils have received increasing attention in recent years as an alternative source of fuel. Transesterification of rapeseed oil to produce rapeseed oil methyl ester improves the oil for use as a fuel. Rapeseed oil methyl ester is probably the most common form of 'bio-diesel' produced, particularly in Europe. Subject to economic considerations, there may be a continued expansion of this market as the benefits of this fuel become more widely known (Poulton; Körbitz, 1995). The chemistry of rape seeds is described in more detail in Section 2.2

1.4 DISTRIBUTION AND PRODUCTIVITY IN UK AND EUROPE

1.4.1 TRENDS IN UK PRODUCTION

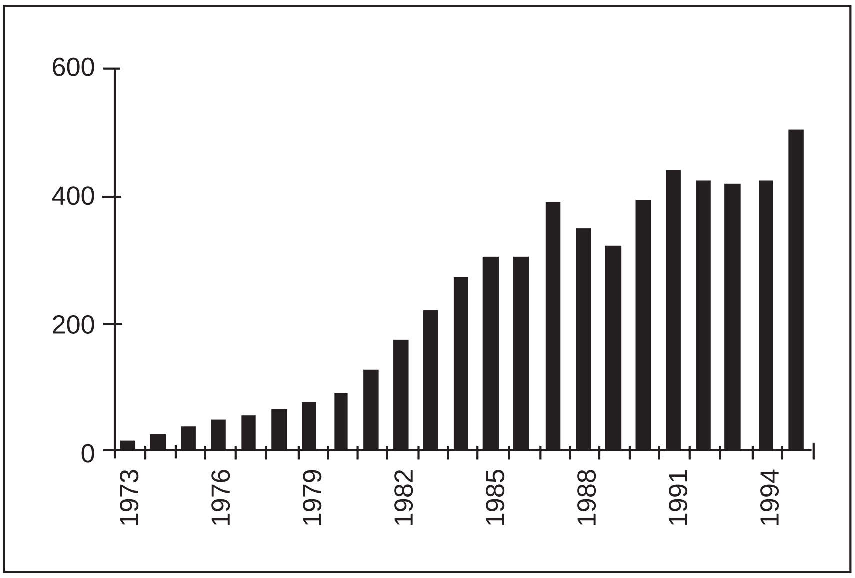
There has been a dramatic increase in the quantity of oilseed rape grown in the UK over the last twenty harvest years. The changes in production from the early 1970s to 1995 are shown in Figure 1.1. Data for this graph have been taken from Ward *et al.* (1985) and the 'Agriculture in the UK' annual reports produced by the Ministry of Agriculture, Fisheries and Food (MAFF).

Throughout the 1960s only a small amount of oilseed rape was produced in the UK (between 2000 and 15 000 tonnes annually) and it was not until 1973 that there was the first large increase in production. This increase was due, in part, to the higher yield that could be obtained from new winter varieties that rapidly superseded the spring ones. The introduction of these high yielding winter varieties was interrupted by the realisation that high erucic acid and glucosinolate levels were undesirable (Ward *et al.,* 1985). Varieties which produced oil low in erucic acid (single-lows) were introduced in the late 1970s and then double-low varieties (see Sections 1.1 and 2.2) followed.

Throughout the 1970s the main areas of production were in Eastern England and the East Midland counties, however, in the early 1980s, there was a northward expansion into Northern England and Scotland (Ward *et al.,* 1985). The distribution of oilseed rape areas in Great Britain for 1995 is shown in Figure 1.2.

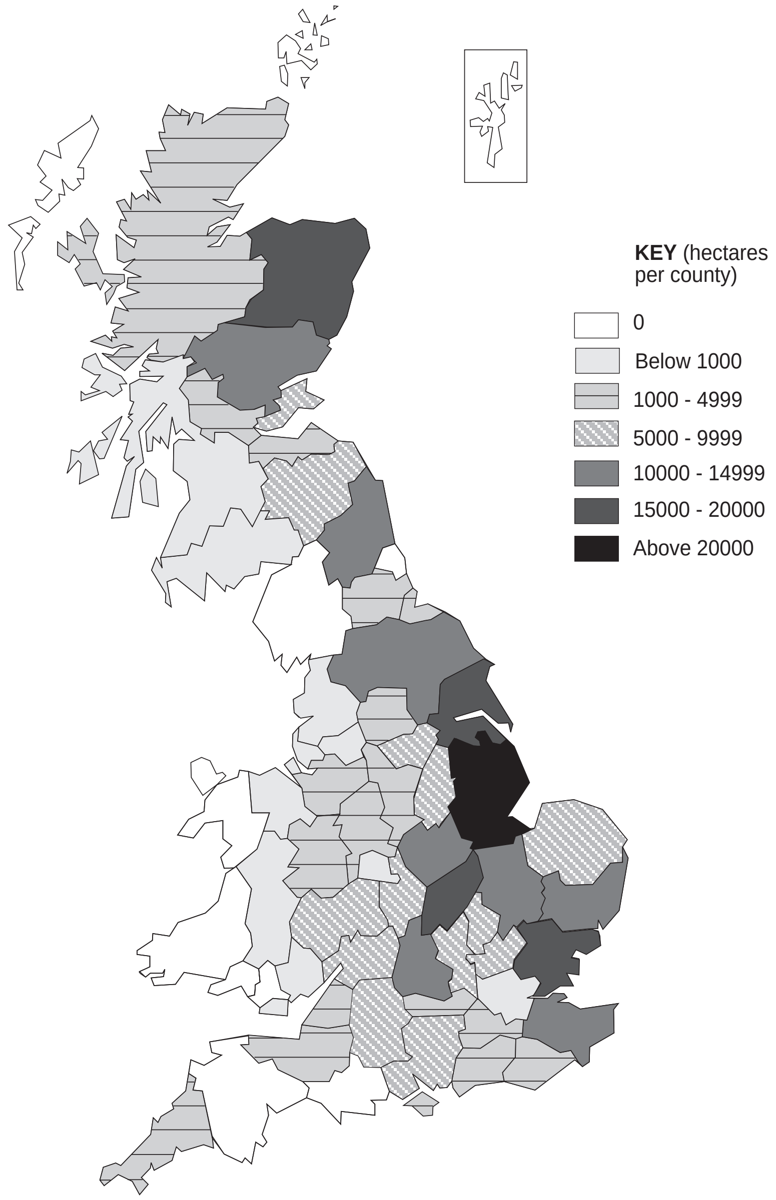
The amounts of autumn and spring sown oilseed rape produced in England between 1991 and 1995 and in Scotland between 1988 and 1996 are presented in Table 1.1a and 1.1b, respectively, and a regional breakdown of oilseed rape production for England and Wales in 1995 is presented in Table 1.2. The data presented here were compiled by MAFF. It should be noted that the derivation of the data is different in each of the tables, accounting for differences in estimated production between tables.

Figure 1.1 Changes in UK production of oilseed rape



Data sources, 1973–1985 Ward *et al.* (1985); 1986–1995 MAFF (Agriculture in the UK, HMSO).

Figure 1.2 Oilseed rape areas (excluding industrial non-food use on set aside) for Great Britain 1995



Adapted from figure supplied by MAFF (Source: 1995 Agricultural and Horticultural Census)

Table 1.2 Production in hectares of crop grown of oilseed rape and other *Brassica* crops for 1995 in the MAFF regions of England and Wales

MAFF Region	Rape grown for oilseed	*Brassica* crops for stock feeding*	
		Turnip & Swede	Kale, Cabbage, Savoy, Kohl Rabi & Rape
North Region	19 088	3 009	783
Yorks & Humberside	39 588	1 192	981
East Midlands Region	73 361	384	1000
East Anglian Region	31 726	162	490
South East Region	86 490	246	1530
South West Region	26 057	3874	3243
West Midlands Region	20 573	1216	751
North West Region	2884	338	140
Wales	1578	1576	1184

Data taken from MAFF 1995 Agricultural and Horticultural Census.

* Other *Brassica* vegetables for human consumption accounted for a further 47 000 ha in the UK in 1995 (data supplied by MAFF)

1.4.2 MAJOR OILSEED RAPE VARIETIES GROWN IN THE UK

Throughout the history of oilseed rape production in the UK there have been many different varieties grown. The common pattern has been that varieties have been introduced, grown for a few years, and then replaced by new ones.

The European Community (EC) rules governing the Arable Area Payments Scheme (introduced in 1992) specify that growers of double-low rapeseed must use varieties from a list in the EC regulations to be entitled to area payments. The list currently names 286 varieties including varietal associations (e.g. composite hybrids) and new varieties are added regularly. There is no equivalent list for high erucic acid rapeseed varieties. Similarly developmental (trial) varieties of rapeseed are also eligible for support, subject to meeting certain criteria.

One way to assess the relative amounts of different varieties grown in the UK is to look at seed production figures. For 1995, nine varieties comprised 94% of the seed that was available for processing and sowing in the autumn, with one variety, Apex, comprising 54% (NIAB, 1996).

1.4.3 PRODUCTION IN EUROPE

Data for oilseed rape production within Europe from the harvest of 1993 to the estimated harvest in 1996 are presented in Table 1.3. These data include both production under set-aside and under the Arable Area Payments Scheme. Presently, of the 15 EC countries, Germany, France and the UK produce the most, with Germany producing nearly twice as much as the UK.

Table 1.3 Estimated area of oilseed rape production across Europe. Units are 1000 ha

	Harvest year		
Country & EC totals	1994	1995	1996[a]
Luxembourg & Belgium	15	12	8
Denmark	171	156	150
Germany	1082	1003	1020
Spain	69	87	60
Greece	0	0	0
France	702	862	873
Ireland	6	3	1
Italy	14	44	64
Netherlands	1	2	2
Portugal	0	1	1
UK	506	441	419
EC12 (pre 1995)	2567	2610	2598
Austria	71	96	78
Finland	67	85	77
Sweden	128	102	85
EC15 (post 1995)	2834	2894	2838

Data provided by MAFF based on European Commission Sources

Note: Includes Setaside Scheme (industrial non-food use) and Arable Area Payments Scheme (industrial and food use)

[a] latest estimate

2 Chemistry of oilseed rape

2.1 INTRODUCTION

The chemistry of the *Brassica* oilseeds is reviewed in detail in Uppström (1995). Nutritionally, the oils produced by rape are probably of most interest for the production of edible oil. Rape is also a good source of protein, and contains significant amounts of carbohydrate and fibre.

The seeds are high in protein, particularly the storage proteins napin and cruciferin, and the structural protein oleosin, which accumulate during seed development. Polysaccharides are the major carbohydrates present in the mature seed; soluble carbohydrates, monosaccharides and oligosaccharides occur in smaller amounts. The polysaccharides have been at least partially characterised as amyloids, arabinans, arabinogalactans, pectins, starch and lignins.

The nutritional quality of the seed is influenced by the amounts of other compounds present including the phenolics, phytates and glucosinolates. Volatile organic compounds (VOCs) are produced by *Brassica* oilseed plants and have been investigated as a possible cause of human health effects. These are described in more detail in Section 2.3.

2.2 EDIBLE OILS

In industrial terms, a press or solvent extract of vegetable seed is referred to as an oil if it is liquid at room temperature, and fat if it is hard. (Biochemists tend to use a different definition and refer to such extracts as lipids, due to their solubility in certain organic solvents or their derivation from long-chain fatty acids). On average, oilseed rape yields 3 tonnes/hectare of seed of which about 40% by weight is oil (OECD, 1994). In the case of oilseed rape, triacylglycerols constitute more than 90% of the oil. Smaller amounts of partial glyceride (about 1%), mono- and diacylglycerol and free fatty acids (<0.5%) may also be present, although they usually only occur in significant amounts when the plant is damaged. Polar lipids, phospholipids and galactolipids constitute about 4% to 5% of the seed oil when extracted with a polar solvent such as chloroform-methanol, but only about 2% to 3% in crude oils extracted commercially with less polar solvents such as *n*-hexane (Uppström, 1995).

Triacylglycerols are composed of three fatty acids esterified at the hydroxyl positions of glycerol. The fatty acid composition of the triacylglycerols is an important factor determining the industrial or food value of the oil. The properties and value of fatty acids depend on the number of carbon atoms in the molecule (chain lengths) and the number of double bonds present (level of unsaturation). Traditionally, oilseed rape has contained significant levels of the long-chain fatty acids, eicosenoic acid and erucic acid. Experiments indicated that the nutritional value of oilseed rape would be greatly enhanced if the level of erucic acid was reduced and varieties have now been developed that have low erucic acid content (<2%) (single-low varieties) and glucosinolate content (double-low); these varieties are valuable as a source of edible oil. Furthermore, levels of linolenic acid have been reduced in order to improve the storage characteristics of the oil, and levels of linoleic acid have been increased to improve nutritional value. Varieties producing oils with these characteristics have been generated by selective breeding; in the future genetic manipulation may help produce oils for specific markets and uses. Oils rich in long-chain fatty acids, particularly erucic and behenic, are used in industry to produce non-food products (see Section 1.3) (Uppström, 1995).

2.3 VOLATILE ORGANIC COMPOUNDS

The identity of VOCs emitted from oilseed rape has been determined in many different studies (Tollsten & Bergström, 1988; Evans & Allen-Williams, 1992; Robertson *et al.,* 1993; Butcher *et al.,* 1994; Blight *et al.,* 1995; Butcher *et al.,* 1995). Brief descriptions of the three main studies by Tollsten and Bergström (1988), Robertson *et al.* (1993) and Butcher *et al.* (1994) are provided below. The studies by

3 Air pollution and pollen

3.1 POLLEN LEVELS AND DISPERSAL

Several studies have considered the dispersal of pollen from oilseed rape crops, to evaluate both the risk of gene transfer from transgenic crops to feral populations and exposure of humans to pollen. These studies have used various forms of spore traps to determine the dispersion of pollen away from the field. Models have also been applied to the data collected to predict the capacity for spore dispersal.

McCartney and Lacey (1991) studied the production and dispersal of oilseed pollen in crops grown in field situations at Rothamsted Experimental Station from 1985 to 1989. Pollen levels within crops were measured using a 7-day pollen recording spore trap. In three of the years the relationship between height above the crop and pollen levels was investigated using rota traps. These rota traps were also placed at different distances from the edge of the field.

Pollen production was found to last from 30 to 40 days between April 28 and June 14, although the time of onset differed between years. Pollen levels varied greatly on a day to day basis, but produced a bell-shaped curve (reflecting increase and decline in flowering) when 11-day running averages were plotted.

The relationship between weather and pollen levels was also investigated. Wind-run (km) and to a lesser extent solar radiation were related to pollen counts, accounting for between 8% and 38% of the variance in each dataset and 19% in the averaged dataset. Although pollen levels were not correlated with rainfall, counts on wet days were usually less than those on dry days. Mean 24-hour counts on wet days were significantly lower than dry days, for the combined 5-year data set. Virtually no pollen was trapped at night and generally pollen levels peaked at mid afternoon. The greatest hourly average pollen count observed was 2800 grains/m^3, but usually maximum values were between 600 and 1000 grains/m^3.

3.2 FUNGI PRODUCING AIRBORNE SPORES ASSOCIATED WITH OILSEED RAPE

There are a number of fungal pathogens of oilseed rape and other species of Brassicaceae which are known to be dispersed by airborne spores (Gladders, 1984). McCartney and Lacey (1992) listed *Alternaria brassicae*, *Botrytis cinerea*, *Peronospora parasitica* and *Pyrenopeziza brassicae* as prime examples. A small number of studies have investigated the airborne fungal spores associated with oilseed rape crops, including temporal changes in airborne levels, and the effects of seasonal and environmental conditions (McCartney *et al*., 1986; McCartney & Lacey, 1992; Soutar *et al*., 1994).

The distribution of light leaf spot disease, which is caused by *Pyrenopeziza brassicae*, is more widespread in Scotland and Northern England than in Southern England. This is probably due to climatic factors (Thomas & Walker, 1994). The incidence of the disease also fluctuates from year to year (NIAB, 1996).

McCartney *et al*. (1986) investigated the dispersal of *Pyrenopeziza brassicae* spores from an oilseed rape field. The pattern of decrease of spores away from the edge of the field, downwind, was approximately exponential, with the concentration at ground level decreasing by half in a distance of between 7 and 10 metres from the field edge. Spore concentration decreased approximately exponentially with height above the field so that the concentration between 1 and 1.5 metres above the crop was about half that at the top of the crop. Wind speed and vertical profile spore data collected on four separate days in July and August were used to calculate a rate of loss of *Pyrenopeziza brassicae* spores from the

3.3 INTERACTIONS BETWEEN POLLEN AND POLLUTION

The air pollutants that occur during the pollen season for oilseed rape in the UK differ markedly geographically, but could include sulphur dioxide, ozone, nitrogen oxides and particulates of various types. The dispersal of wind blown pollen and pollution are both influenced by the same general factors. Warm, dry days with moderate winds are conducive to high concentrations of air pollutants and pollen, so they are likely to coincide at a local level. Little work has been conducted on interactions between pollutants and the pollen of oilseed rape, but research on other plants has found that pollutants may have effects on pollen size and morphology and also on the allergenicity of pollen proteins. The effects operate through two main routes. The first of these is indirect. Stress on plant growth caused by pollution can lead to reduced net productivity resulting in smaller, fewer pollen grains and an increased number of deformed grains (Omura *et al.,* 1989; Troumbis, 1990). However, the allergen load per weight may be increased due to a physiological stress response. (Described for birch pollen by Breitender & Scheiner, 1990). Secondly, direct contamination of pollen may occur, either on the plant or in the air. Research conducted on this aspect to date is limited, but has indicated that various interactions may take place that are significant in altering the allergenicity of pollen. The main aspects are summarised below, but most are unlikely to be important for oilseed rape pollen in the ambient atmosphere, because it is relatively heavy and most of it does not travel far in the air (see Section 3.1). Consequently it has only a short travel/exposure time.

Particles may adhere to the surface of pollen (Behrendt *et al.,* 1992; Bessonova *et al.,* 1992). In the case of vehicle exhaust this may induce an enhanced response to allergen (Ishizaki *et al*., 1987). Oilseed rape pollen is sticky and could collect particulates efficiently during its flight, but it is unlikely that vehicle exhaust particulates would be abundant in agricultural areas. Allergenic protein from pollen may be transferred to pollution particles by various mechanisms. These particles are likely to be smaller and have different dispersal mechanisms to those

4 Agrochemicals

4.1 PESTICIDES USED ON OILSEED RAPE

A wide range of pesticides are used on oilseed rape in the UK, however, the chemicals involved are also used on other arable crops beside oilseed rape. Data reported here are based on surveys of pesticide usage on arable farm crops in Great Britain for 1994, published by MAFF and the Scottish Office Agriculture Fisheries Department (Garthwaite *et al.*, 1994). On average, each oilseed rape crop received two herbicide sprays, one fungicide spray and one insecticide spray.

Within this review a number of criteria have been applied to identify the pesticides most widely used on oilseed rape, during and after flowering. This is the most relevant time period with respect to reporting of adverse health effects. These pesticides are mainly fungicides and insecticides. A number of herbicides are also used on rape crops but these are generally applied before the flowering period and so have not been included.

The selection criteria were:

❒ usage on oilseed rape was on 10 000 hectares or more in Great Britain in 1994 (latest published MAFF Pesticide Usage Survey);

❒ the pesticide is applied as a spray;

❒ application is likely to be sometime between the onset of flowering (at or after 'green-bud' stage) and harvest.

The final selection of pesticides for consideration is presented in Table 4.1, which summarises the principle uses of each pesticide and indicates their known potential to cause eye and skin irritation. Possible interrelationships between irritants, allergens and asthma are considered in Section 6.

Table 4.1 Main pesticides used on oilseed rape from onset of flowering to harvest, with information on their uses and potential to cause irritation

Pesticide	Classification	Target organisms /diseases with respect to oilseed rape	Irritant[a]	
			Eye (mucous membrane)	Skin
Fungicides				
Carbendazim	systemic benzimidazole fungicide	*Botrytis*, light leaf spot	N	N
Flusilazole	systemic, protective & curative conazole fungicide	light leaf spot	M	M
Iprodione	protectant dicarboximide fungicide	*Alternaria, Botrytis, Sclerotinia* stem rot	N	N
Iprodione/thiophanate methyl	protectant & systemic fungicide	*Alternaria, Botrytis, Sclerotinia* stem rot, grey mould, stem canker	M[b]	M[b]
Maneb	protectant dithio carbamate fungicide	*Alternaria*		
Prochloraz	conazole fungicide			
Sulphur	broad-spectrum fungicide & foliar feed	foliar feed		
Tebuconazole	systemic conazole fungicide	*Alternaria,* light leaf spot, *Sclerotinia* stem rot	N	N
Vinclozolin	protectant dichloranilide fungicide	*Alternaria, Botrytis, Sclerotinia* stem rot	S	M

Some of the pesticides listed, particularly the insecticides, will have some toxicity to bees and this may affect how they are used during peak flowering. In particular, approved use of the insecticides α-cypermethrin, cypermethrin, deltamethrin, and triazophos on flowering oilseed rape crops would be limited to times when there is minimum risk to foraging bees.

During the pesticide registration process, the potential health effects of a given pesticide are carefully considered by extrapolating from animal data and estimating exposure. Where necessary, special statutory instructions are indicated on the label of the pesticide to reduce the risk to both the operator and the public to an acceptable level.

Four of the pesticides used on oilseed rape have been evaluated in the World Health Organization (WHO) Environmental Health Criteria Series. WHO has concluded that carbendazim is unlikely to cause systemic toxic effects either in the general population or in occupationally exposed subjects (WHO, 1993); when cypermethrin is applied according to good agricultural practice, exposure of the general population is negligible and unlikely to present a hazard (WHO, 1989a); the risk of exposure of the general population to α-cypermethrin is negligible if good agricultural practices are followed (WHO, 1992); and the exposure of the general population to deltamethrin is likely to be very low and is not expected to pose a hazard under recommended conditions of use (WHO, 1990).

5 Equine pathology

In a 13 year old thoroughbred mare from the Tayside region of Scotland (a region with areas abundant in oilseed rape), exacerbation of symptoms of chronic obstructive pulmonary disease (COPD), which is associated with the housing of horses, particularly in the presence of mouldy forage and bedding and poor ventilation, was reported in one particular year when the horse was put outdoors in the spring of 1987. In other years symptoms had generally improved when the horse was put outdoors (Dixon & McGorum, 1990). An outdoor allergen, possibly pollen from nearby rape fields, was suggested as a potential cause of the problems. Although symptoms were alleviated when the horse was moved away from possible pollen sources they were exacerbated during both flowering and harvesting of nearby rape crops. No antibodies to oilseed rape pollen were found on serological examination.

To examine further the relationship between oilseed rape and pulmonary disease in horses, McGorum and Dixon (1992) examined the effects of oilseed rape on asymptomatic horses, symptomatic horses with COPD and control horses. The horses were exposed either by being put in a field of flowering *B. campestris* for six days (2 asymptomatic, 3 symptomatic, 2 control), or by inhalation challenge (3 asymptomatic, 3 symptomatic, 2 control) with freshly collected *B. napus* pollen or by nebulised inhalation challenge with a commercial extract of *B. napus* pollen. Intradermal testing was also carried out using the commercial extract of *B. napus* pollen on all eight horses and a further 12 horses. Arterial blood gas and pH was analysed, pulmonary function was assessed and bronchoalveolar lavage was examined cytologically.

The challenges had no significant effect on any horse and no clinical signs such as head shaking, dermatitis or parotid swelling were observed. However exacerbation of the pulmonary disease in some symptomatic horses with COPD was observed following inhalation challenges with fresh *B. napus* pollen and *B. napus* pollen obtained from a commercial source. No positive response was obtained to the intradermal tests. The authors suggest that while exposure to oilseed rape does not appear to be a major cause of respiratory disease in horses, it may exacerbate pulmonary disease in some horses with COPD.

6 Health effects of oilseed rape

6.1 INTRODUCTION

Oilseed rape has been grown in the UK for many years, but it became a major arable crop in the 1980s. The general description and uses of oilseed rape have been discussed in previous chapters. Since the late 1980s there has been increasing public concern with regard to oilseed rape and its possible potential to cause adverse health effects. In contrast, it should be noted that intensive cultivation of other vegetable brassicas such as cabbage, cauliflower and Brussels sprouts (see also Table 1.2) has taken place near homes for many years without concern. Nonetheless, allergic type reactions, such as, itching eyes, skin irritations, cough, headache, runny nose, tightness of chest, breathing difficulties and a general feeling of being unwell have been reported among people living beside or close to oilseed rape fields. Exacerbation of these symptoms has been reported at peak flowering times.

Hypersensitivity to oilseed rape pollen was first reported in Sweden in the 1950s (Colldahl, 1954). A 30 year old farmer with no previous history of allergy exhibited classical symptoms of an allergic reaction. When the rape began to bloom in May 1951 he presented with an itchy nose, increased nasal secretions and sneezing. Itching and congestion of both eyes also occurred followed by wheezing some three weeks later. The symptoms increased in intensity every time he approached a field in bloom. During the first year these symptoms also occurred at night. A rape field was situated 30 metres from his bedroom, which was on the windward side of the house facing the rape field. The following year when the rape began to bloom the symptoms reappeared but not with the same severity, the authors suggested this was possibly due to the fact that the rape field was situated some 250 metres from his house. The patient was desensitised by treatment with increasingly concentrated rape pollen extracts.

ALLERGENS AND IRRITANTS

Allergens and irritants interact in several ways. Firstly, both may cause asthma; allergens by sensitisation and irritants by an unknown mechanism. Irritant-induced asthma has been termed 'reactive airways dysfunction syndrome' (Brooks *et al.,* 1985). Secondly, irritants such as tobacco smoke, ozone and other agents can potentiate allergic sensitisation in animals (Zetterström *et al.,* 1985; Biagini *et al.,* 1986; Matsumura, 1970) and there is evidence that this occurs with some, though not all, occupational exposures to inhaled aeroallegens (Cartier *et al.,* 1984; Venables *et al.,* 1985; Venables *et al.,* 1989). Thirdly, both allergens and irritants may provoke an asthma attack in an individual with pre-existing asthma. In the case of allergen, provocation only occurs in an individual specifically sensitised to that allergen. Irritants are non-specific provocants of asthma. Fourthly, concurrent exposure of a sensitised individual to the relevant allergen and also an irritant leads to enhancement of the allergen-provoked asthmatic response compared to challenge with allergen alone (Molfino *et al.,* 1991, Devalia *et al.,* 1994).

A limited number of studies have investigated the relationship between oilseed rape and allergenicity and/or irritancy and these are summarised below.

6.2 SENSITISATION TO OILSEED RAPE POLLEN

6.2.1 POPULATION STUDIES

SCOTLAND

As reported in an abstract, Packe *et al.* (1992) examined the association of respiratory symptoms that developed in early summer during the oilseed rape flowering season, among 28 subjects from the Grampian area of Scotland, where the crop is intensively cultivated. Seventeen cases (average age 34 years) skin test to oilseed rape pollen alone and this worker had spent four years in close contact with oilseed rape. Of the nine who were skin test positive to oilseed rape pollen, five were RAST positive and these five also responded positively to the nasal challenge. VOCs were used in the nasal provocation test, but the results were unclear because of the high concentration of ethyl alcohol used to dissolve the VOCs. [A small nasal challenge study, conducted within the larger study, is difficult to interpret because of lack of clarity in reporting. Both non-allergic controls and the symptomatic subjects showed nasal symptoms.]

Pollen counts were taken on a daily basis from the middle of the rural community served by Deddington Health Centre. Even on the peak day for oilseed rape pollen, 14 May 1989, pollen counts were higher for other allergens (oilseed rape, 90/m^3 of air; pine, 480/m^3; *Alternaria,* 480/m^3; mugwort, 96/m^3; silver birch, 96/m^3; grass, 450/m^3; *Cladosporium,* 360/m^3; nettle, 300/m^3). The authors concluded that allergy to oilseed rape was not a common phenomenon in the general population, where it occurred only in atopic individuals who were already allergic to other airborne pollens. The same appeared to be true in those occupationally exposed, with the exception of one worker who had worked closely with the plant for four years.

6.2.2 CLINICAL STUDIES ON OILSEED RAPE AND ALLERGY

Parratt *et al.* (1990) investigated sensitisation to oilseed rape and other common allergens using serum samples collected in Dundee and Glasgow. In Dundee, 175 samples were collected between May and September 1988 and a further 82 samples were collected during November and December 1988. These were compared with 141 samples from Glasgow, collected during February, June and July, 1988. February and September both lie outside the rape flowering season. Samples were tested for mixed grasses, house dust mite (*Dermatophagoides pteronyssinus*), cat and dog dander, mixed foods, oilseed rape and mixed moulds (*Penicillium notatum, Cladosporium herbarum, Aspergillus fumigatus* and *Alternaria alternata*) by RAST; total IgE levels were also measured. Mixed moulds were tested because the cut rape may be left in the fields for several weeks before harvesting and may become mouldy during that time.

Table 6.3 Sources of oilseed rape pollen extracts

Study	Country	Nasal Provocation Test	Skin Prick Test	RAST
Bucur & Arner (1978)	Sweden	–	NS	–
Parratt *et al.* (1990)	Scotland	–	–	Pharmacia (phadebas)
Fell *et al.* (1992)	England	Allergon (Sweden)	Dome Hollister Stier (Bridgend, UK)	Pharmacia (Milton Keynes, UK)
Soutar *et al.* (1995)	Scotland	–	NS	NS
Hemmer *et al.* (1997)	Sweden	–	ALK Soluprick no 317 (Denmark)	Pharmacia (Sweden)

NS - Not Specified

6.2.3 CLINICAL STUDY ON FUNGAL PATHOGENS AND ALLERGY

A study by Galloway (1996), reported in a thesis, investigated the role of fungal pathogens of oilseed rape, *Alternaria alternata* and *Botrytis cinerea*, as possible causes of oilseed rape related allergy. The study was conducted in 1989 and 1990 in the Letham/Bowriefauld area of Angus in Tayside, an area with over 6000 hectares of oilseed rape. A total of 73 people took part in 1989 and 63 in 1990. Participants were randomly selected by approaching householders in the Angus area who were asked to fill in daily diary cards to record symptoms similar to hay fever, scored on a scale of one to ten. Symptoms consisted of sneezing, blocked nose, runny nose, wheezing cough, headache, chest tightness and eye irritation. Individuals' allergic status was determined by the medical history and the number of positive skin tests to common allergens. Participants needed at least two positive skin tests to be classified as allergenic. The participants were divided into four groups. Group 1 was classified as non-allergic, rape pollen skin test negative, group 2 as allergic, rape pollen skin test negative, group 3 as non-allergic, rape pollen skin-test positive and group 4 as allergic, rape pollen skin-test positive. There was only one individual in group 3. Serum from each participant was used for IgG immunofluorescence and RAST. Control sera were obtained from the blood transfusion service in Glasgow, an area where very little oilseed rape is

6.3 VOLATILE ORGANIC CHEMICALS

The emission of VOCs from any plant source must be seen as a common and largely natural phenomenon. Different plant species essentially produce similar compounds, although some are specific to the species and often characteristic of the family. The compounds involved are mostly detectable by human olfaction.

A broad range of VOCs typically produced by plants, including species-specific compounds, fall into the general scheme outlined in Figure 6.1. For some compounds, irritancy and toxic effects, which are dependent upon exposure duration can be manifested at levels below the saturated vapour concentration. Nonetheless, for the VOCs, olfactory detection generally occurs at concentrations that are lower than those required for physiological effects by at least several orders of magnitude (WHO, 1989b; Takeoka *et al.,* 1996). Human perception of VOCs from plants in natural and agricultural ecosystems usually occurs subliminally, either because of the low levels present or because of psychological habituation. However, under special circumstances, plant VOCs are perceived; the most obvious circumstances are when consuming plant material as food, when sniffing flowers, or when encountering agricultural activities that specifically release these compounds, such as the cutting of hay/silage or the felling of trees, particularly conifers. High monoculture biomasses can give a relatively greater concentration of VOCs close to the plantation, such as would be the case for a pine forest or a flowering crop. Flowering plants have evolved so as to attract pollinators by combinations of visual and olfactory cues. These usually remain, even where other mechanisms of pollination are utilised. Prominent crops, with regard to olfactory perception arising from VOCs generated by flowers, are field beans and oilseed rape; the former is generally more readily perceived.

1985). Allergic contact dermatitis and contact urticaria have also been reported (Mitchell & Jordan, 1974; Blaiss *et al.,* 1987; Dannaker & White, 1987; Kavli & Moseng, 1987). Isothiocyanates in the mustard oils have been suggested to be responsible for these allergic reactions (Meding, 1985; Dannaker & White, 1987). A woman who developed acute dermatitis of her hands after chopping salad plants patch tested positive to radish (*Raphanus*) and to allyl isothiocyanate and benzyl isothiocyanate (Mitchell & Jordan, 1974).

Terpenes such as linalool, *d*-limonene and β-pinene are found in low concentrations in products such as soap, detergent, creams and lotions (usually <0.05%; maximum 0.3%) and perfumes (usually about 0.3%; maximum 1.5%). Sensitisation to these compounds was not found when tested in human volunteers at concentrations ranging from 8–20% in petrolatum (Opdyke, 1975a, b; Opdyke, 1978). Small quantities of terpenes released from rubber gloves have been demonstrated to induce asthma attacks (Seaton & Cherrie, 1988) and short-term terpene exposure induces an increase of the macrophages and the mast cells in bronchoalveolar fluid (Johard *et al.,* 1993). Sarlo and Clarke (1992) and Gauggel *et al*. (1993) have shown that some VOCs can haptenate carrier proteins and Sarlo and Clarke have demonstrated an immune response when these haptenated proteins are injected into guinea pigs. Sensitisation of these animals *via* inhalation exposure has also been demonstrated.

6.4 SUMMARY

Among population studies that have investigated the presence of specific IgE to oilseed rape, a study conducted in the Grampian region of Scotland, to validate findings from an earlier questionnaire study, found only one subject with a positive RAST for oilseed rape among 22 cases of conjunctivitis or respiratory symptoms reported during the oilseed rape flowering season (Soutar *et al.,* 1995). Similarly in a further study of 1478 residents in an English rural area where oilseed rape was grown, only three subjects, out of the 24 who considered their symptoms were due to oilseed rape, had positive RAST or nasal provocation tests to oilseed rape (Fell *et al.,* 1992). The latter study did, however, find a higher

7 Conclusions

There have been a number of reports, both epidemiological and clinical, that have investigated a possible association between exposure to oilseed rape and symptoms of allergenicity and irritancy. **Based on these reports there is evidence that some people may have an allergic response to oilseed rape pollen, although it appears that the response is largely confined to atopic individuals. The available evidence suggests that sensitisation to oilseed rape pollen alone, in the absence of sensitisation to other pollens or other common allergens, appears to be rare.** Although it is possible that exposure to oilseed rape may cause an increase in the incidence of symptoms experienced by atopic individuals, there is no evidence to suggest that the kinds of symptoms experienced will be any different from, or more intense than, those caused by other allergens. Thus only a few, mainly atopic, individuals in populations which are in close proximity to oilseed rape are likely to be affected and there appears to be no exceptional public health problem in comparison with responses to other pollen allergen sources.

Currently available data suggest that allergic responses to oilseed rape make very little contribution to the overall burden of allergy in the UK and diagnoses of pollen allergy should be considered in the context of an increasing prevalence of allergy in developed and developing countries. On the basis of its size and very limited distribution into the air, oilseed rape pollen does not generally contribute greatly to the total amount of pollen present in the general environment at the time oilseed rape flowers.

Although oilseed rape emits many VOCs, evidence indicates that the VOCs produced are essentially similar to those of other flowering plants. However, the relative proportions of VOCs will be different and it is possible that the amount produced per unit area may be large, relative to other crops, due to the densely flowering heads of oilseed rape. There are limited data on the concentration of VOCs in oilseed rape fields and surrounding areas or, indeed, from cultivated or natural biomass generally. Furthermore, there appear to be few differences between the ranges of VOCs produced by the different oilseed rape varieties currently commercially available. **On the basis of currently available data there is no direct evidence to suggest that VOCs are responsible for the adverse health effects reported to be associated with oilseed rape.**

8 Future research

8.1 KEY AREAS FOR FUTURE RESEARCH

In attempting to assess the importance of any health impact associated with exposure to oilseed rape, consideration should be given to the relative costs and benefits of protecting a small number of people from possible health effects and the economic importance of the crop, both to growers and the general population.

It is still not clear to what extent the adverse health effects sometimes reported in association with oilseed rape are due to the pollen itself, other factors associated with the crop, confounding factors not connected with the crop (such as elevated ozone levels coincident with the time period of flowering), the influence of other determinants such as colour and smell on perceived impact, or interactions between any of these.

Studies of allergenicity reported to date have used numerous oilseed rape extracts produced commercially or independently, which are very variable in quality and have not been standardised or validated. Standardised extracts should be developed, preferably using several of the most commonly cultivated varieties of oilseed rape.

Before it will be possible to ascertain definitively whether or not VOCs emitted by oilseed rape are a possible cause or contributory cause of adverse health effects, studies are needed to estimate likely concentrations or to measure actual levels of VOCs in oilseed rape fields. It would then be pertinent to undertake chamber studies with VOCs emitted from oilseed rape at concentrations similar to those most usually found in the field.

A major way forward to clarify any possible relationship between oilseed rape and factors associated with its production and adverse health effects will be to conduct controlled challenge studies. Such studies should be conducted among volunteers from susceptible groups such as atopics or those with positive skin prick tests to oilseed rape pollen, among people with apparently non-allergic responses to oilseed rape or associated factors, and among individuals with no apparent response to the

8.2 SUMMARY OF RESEARCH RECOMMENDATIONS

ASSESSMENT OF HEALTH EFFECTS

❒ Develop standardised oilseed rape pollen extracts for use in epidemiological and challenge studies

❒ Conduct volunteer studies, including chamber studies in atopic, symptomatic and asymptomatic individuals to determine whether levels of VOCs and/or fungal spores associated with oilseed rape can cause adverse effects, to investigate the incidence of monosensitisation to oilseed rape pollen, and to investigate interactions between pollen and common air pollutants

❒ Undertake well defined epidemiological studies, following potentially susceptible groups, such as atopics, intensively throughout the season, monitoring symptoms in conjunction with environmental factors (pollen, VOCs, fungal spores, air pollutants, submicronic particles, agrochemicals) over time and incorporating 'quality of life' measurements

EXPOSURE

❒ Clarify the distribution of oilseed rape pollen and antigenic particles in rural communities in relation to other sources of pollen and to distance from the crop

❒ Investigate the interactions of particles derived from oilseed rape pollen with other air pollutants, paying particular attention to the effect on transport

❒ Conduct quantitative or more sophisticated qualitative investigations of the concentrations and relative proportions of VOCs produced by oilseed rape fields and the dispersal of VOCs from the fields

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