POISONS IN PLANTS : SOME BIOLOGICAL AND HUMAN IMPLICATIONS

Convocation Address

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This is meant to be a sort of welcoming address to you new graduates in statistical topics. All of us older people here do indeed hope that you will find good use in the future years for what you have been learning here, and that you will enjoy the happiness that comes with work well done.

This Institute has a good tradition, apparent in its motto, of never allowing statistics to get detached from real life. Agriculture and human nutrition are full of pressing problems for the people of India. The teaching and research work going on in the Institute have helped to introduce you to some of these. No doubt a number of you will take up work in these fields. So, although I am a biochemist and not a statistician, I am not going to apologise for the topic of this address. You may even find some interest in being shown familiar things from an unfamiliar angle.

Large areas of the world are generously covered by vegetation. This represents a considerable mass of potential animal food, and the question arises why it maintains itself as well as it does.

In chemical terms, the nutritional needs of animals can be satisfied by a hundred or so fairly simple chemical substances. To find out what these substances are was one of the big achievements of biochemistry during the first half of this century. Animals can now be maintained in good health through several generations on purely synthetic diets and without their usual associated micro-organisms. Animals have a very conservative biochemistry and therefore, when digested, always yield all of these same substances. So one animal can always live by devouring another animal. Very few animals indeed are poisonous to eat; they have other means, usually fairly obvious ones, of avoiding being eaten. Against micro-organisms they have a very sophisticated set of defences, which includes the antibodies.

Plants can become prickly but they do not have open to them the sovereign means of avoiding being eaten—to counter-attack (if large enough), to run away and to hide.

As plants require such very simple nutrients—just carbon dioxide and inorganic salts—they might in principle have evolved some new kind of biochemistry, so as not to be masses of protein, fat or carbohydrate left lying about for animals to eat. Animals would then, in turn, have had to develop a much more sophisticated biochemistry, in order to be able to get nourishment from such plants. But that is not what has happened. Plants have continued to be rather conservative about producing proteins and fat. Some of them have sophisticated their carbohydrates, to the point of indigestibility . But over and above this, as a group they have gone in for manufacturing the most astonishing variety of chemical substances, of which new ones are continually being discovered. A number of these are known to make the plant containing them unpalatable or poisonous. It is reasonable to assume, when you think of all the animals, parasitic plants, fungi, bacteria and viruses which can attack plants, that quite a lot of these substances which have no known function may be active against some predator or parasite in manners that we are not aware of.

Of course, it is not necessary for a plant to achieve total protection against all predators in order for it to be a successful species. In Britain vast areas of upland country, known as moors, are covered by nearly pure stands of ling heather (*Calluna vulgaris* L.). This is a shrub which is so tough and unpalatable that about only one species of animal eats it for choice, and that is our one endemic species of bird, a gallinaceous bird known as the red grouse (*Lagopus lagopus scoticus*). This,like many other animals, exhibits intensely territorial behaviour, thus limiting the pressure of the species on its food supply. V. E. Wynne Edwards has shown animal species to have a variety of ways of behaviour that serve to adjust population to food supply. So what a plant species needs to achieve is to have only a few species of predators or parasites, which have developed over the ages an evolutionary adjustment to it. Trouble starts when you move species from one part of the world to another, and especially when you start growing crops.

What I am going on to say will be clearer if I give a few examples of individual poisonous substances. I will discuss in each case the range of organisms susceptible, and why the poison does not worry the organism producing it.

(1) *The spore protein of* Bacillus thuringiensis. This is one of the most specialized poisons known, and I am including it, in spite of it not being from a plant, because we should look out for similar cases in plants. Each spore of this bacillus has attached to it a crystal of protein. When eaten by a caterpillar, this protein is partly digested by the enzymes of the caterpillar's gut, and there is formed a specific peptide (a particular fragment of the parent protein molecule) which has the effect

of paralysing movement of the caterpillar's gut. As a result, the caterpillar dies and the bacteria grow in its flesh. The spore protein does not yield this same peptide when digested with enzymes of the mammalian gut, nor does this peptide have any paralysing effect on the mammalian gut. So there is great interest in these materials as an insecticide for spraying on leaves, that should be quite harmless to humans eating the leaves.

(2) *The toxic substances of* Amanita phalloides. This is a toadstool, common in temperate woodlands, which is nearly always fatal for people eating it. The active substances are sort of 'caricatures' of peptides, whose chemical structure has been cleared up by Theodor Wieland. Most remarkably, he has also found in the same toadstool another peptide (antamanide) which will act as an antidote, if given just before the poison. Does this play some part in protecting the fungus from the adverse effects of its own poison? *Amanita phalloides* seems generally poisonous to mammals, but you see slugs eating these toadstools with evident relish.

(3) 2-*Fluoroacetic acid.* This was found in a South African plant (*Dichapetalum* sp.) responsible for poisoning sheep. The publication of this discovery from a South African veterinary laboratory during the 1939-45 war caused consternation in military circles, as it was one of their secret poison gases, on whose properties there was supposed to be a strict censorship. It is extremely toxic to all animals, as it blocks their main pathway of oxidative metabolism. It does not seem to upset plants at all, and by watering pot plants with it you can make them poisonous to insects. Unfortunately, it is just too dangerous a substance to have around in the home, and in Britain its sale was prohibited after it had been on the market for a few years.

(4) *Azetidine*-2-*carboxylic acid.* This is a simple amino acid, found in the much loved but poisonous temperate-woodland plant the lily of the valley (*Convallaria majalis* L.). Azetidinecarboxylic acid seems to be universally poisonous, even to other plants, if you introduce it into them. It acts by the simple expedient of being mistaken for the common amino acid proline, which has a rather similar structure. It thus messes up the structures of proteins by getting incorporated into them instead of proline, as the amino acids of which they consist are being strung together. The lily of the valley has specially developed a less stupid enzyme for its own protein biosynthesis, which can distinguish and reject the azetidinecarboxylic acid.

From these examples you can realise that there is a range of poisons from the very specific to the nearly unspecific. I have avoided mentioning the traditionally known plant poisons, the alkaloids, so as to give some slight impression of the chemical versatility as well. When we think that it is not only animals, but also fungi, bacteria and viruses against which these chemical agents may have to operate, we can see why they are so very diverse. We probably know as yet only a tiny monority of them. There are also poisons active against plants of other species. Then there are germination inhibitors, which may act against seeds in the neighbourhood of a plant's roots, or even control the spacing of its own seedlings.

Now for some of the practical implications of what I have been saying.

First, as concerns *plant breeding*. Over the years, of course, there has been the breeding out of unpalatable constituents of vegetables and fruits, particularly of tannins. This has probably made cultivated varieties more susceptible to pests, but it could scarcely have been avoided. Where the protective substance is not unpalatable, more attention could be paid to not breeding it out. All kinds of qualities are liable to be bred out when the breeder's attention is mainly fixed, as it so often is, on yield and colour. New varieties should be bred and tested in the localities where they are to be grown, and where they are subject to the full pressure of the local pests. I understand there has been trouble on this account when strains of rice bred overseas have been introduced into India.

Second, as concerns *plant protection*. There is a need for fungicides, insecticides, etc. that are more specific in their effects, and not dangerous to human beings. Study of the naturally occurring ones in plants and micro-organisms is likely to be a better line of approach than slavishly to test every available synthetic chemical. That, at any rate, has been the experience with antibiotic drugs used against disease in man and animals over the past 40 years, and I feel it is an approach that could well be intensified by people concerned with plant protection.

Third, as concerns *food processing*. Where it is practicable, it may give better protection to the plant to stick to varieties with toxic constituents and then eliminate these during the processing. This is traditional with tapioca. In this country, it has recently been discovered that the nerve poison in *khesari dal* (*Lathyrus sativus* L.) is a water-soluble substance, N^3-oxalyl-L-2,3-diaminopropionic acid. The simple expedient of throwing away the water in which the seeds have been boiled seems to be effective in getting rid of the poison. There are innumerable traditional treatments for improving the nutritive quality of soya beans, which is probably adversely affected by the presence in them of an inhibitor of the digestive enzyme trypsin. In recent years, heat treatment in factories has greatly improved the quality of soya bean meal as a food for animals. Similarly, the discovery of a factory method for removing the toxic substance gossypol from cotton seed has changed it from being used only as a fertiliser into an excellent feeding stuff.

Fourth, as concerns *human diet*. We should be incredibly bored with a diet consisting of only the hundred or so necessary chemical substances. We value food for its flavour, its colour and for the feelings which it induces. It is the thousands upon thousands of substances in plants which we have been discussing that largely provide us with these. For example the oil of citrus skins, which we esteem so highly, probably functions as an insect repellent in the living plant. The widely appreciated flavour of garlic is largely due to allicin, a bactericidal substance which is formed when garlic is crushed. Perhaps this is responsible for the common idea that garlic is a protection from infectious diseases. Nearly every plant which contains caffeine has been used for making pleasantly stimulating beverages. I will not go on from diet to drugs, except to remind you that plants have yielded a good number of drugs, both useful and pleasant ones. But we should keep our eyes open for the unexpected. As an example, the substance dopa (L-3(3′,4′-dihydroxyphenyl)alanine) has been known as a major constituent of broad beans (*Vicia faba* L.) for more than fifty years, without being thought to have any particular physiological effect. Yet just recently it has found some use in the treatment of Parkinson's disease, and is now being said to have aphrodisiac side-effects. Many centuries ago, St. Jerome condemned bean eating, for leading people on into amorous adventure.

In conclusion, I want to leave this thought with you. Although we know several thousands of chemical substances occurring in plants, the majority of these occur in only one, or just a few, species. There are at least 250,000 known species of flowering plants alone. Moreover, in searching for biological effects, one has to consider the entire gamut of living organisms with which the plant may come into contact. So it is certain that our knowledge of this field is still extremely rudimentary. I hope that what I have said has convinced you that it is a field worthy of more intensive cultivation.