Chapter 7
Surfactants in Agriculture

Mariano J.L. Castro, Carlos Ojeda, and Alicia Fernández Cirelli

Abstract Adjuvants such as surfactants improve pesticide efficiency by multiple mechanisms. In particular surfactants increase the foliar uptake of herbicides, growth regulators, and defoliants. Therefore, the choice of the adjuvant in an agrochemical formulation is crucial. Surfactants include anionic, nonionic, amphoteric and cationic surfactants. This review describes the role and properties of new adjuvants for agriculture. In particular adjuvants such as glyphosate formulations are modified to decrease ecotoxicity.

Keywords Surfactant formulation • Pesticide • Agriculture • Adjuvant • Plant cell • Glyphosate • Cuticular • Alkyl polyglycosides • Saccharose esters • Chitosan

Contents

M.J.L. Castro • C. Ojeda • A. Fernández Cirelli (✉)
Centro de Estudios Transdisciplinarios del Agua (CETA-INBA-CONICET), Universidad de Buenos Aires, Chorroarin 280, C1427CWO Ciudad de Buenos Aires, Argentina
e-mail: ceta@fvet.uba.ar; ceta@fvet.uba.ar; AFCirelli@fvet.uba.ar; gemini21@chemist.com

E. Lichtfouse et al. (eds.), *Green Materials for Energy, Products and Depollution*, Environmental Chemistry for a Sustainable World 3, DOI 10.1007/978-94-007-6836-9_7,

7.1 Introduction

The world population is projected to continue increasing into the next century. Population growth is assumed to follow the United Nation medium projection leading to about 10 billion people by 2,050. A central question is how global food production may be increased to provide for the coming population expansion. It would be necessary to increase current levels of food production more than proportional to population growth so as to provide most humans with an adequate diet (Kindall and Pimentel 1994).

Agronomic sciences and their different disciplines should be able to supply solution in order to increase food production. Agricultural science includes knowledge of the land, conducted by the geology, geochemistry and soil science, environmental analysis by the ecology, biogeography, bioclimatology, biometeorology and crops sown, with its potential for improvement through the creation of new seed varieties designed for hybridization and genetic modification. Moreover, there are a lot of factors with influence in the crops yields, such as irrigation, drainage, tillage and fertilizer applied to soil. The type of treatment above described improves the physical qualities of soil, while the use of fertilizers improves their chemical qualities. Finally, the fight against pests and weeds through pesticides is of paramount importance within the modern agricultural activity. The agricultural breakthrough occurred during recent decades by the incorporation of new laboratory techniques, statistics, computer science, satellite information. On the other hand, crop modified by genetic engineering produced a huge increase in yields per hectare of different crops. All the disciplines above described are modifying year by year through the incorporation of new technologies.

Top-10 drivers for the changes of the agricultural industry are (Heinemann 2010):

1. Rising number and age of human beings and their nutritional behaviour
2. Increasing competition of food, feed and energy for agricultural outputs
3. Scarcity of water and arable land relative to the rising demand
4. Constantly increasing regulations & requirements for healthiness and sustainability
5. Genetically modified organism (GMO) and precision-farming enabled increase of productivity and quality
6. Higher volatility of demand vs. supply due to political and financials interventions
7. Ongoing commoditization of essential inputs like agrochemicals and fertilizer
8. Beyond consolidation: business model deconstruction and recomposition
9. More and quicker information due to novel media platforms
10. Personalization-driven convergence of health and nutrition

Agrochemical formulations cover a wide range of systems forms for crop protection that are prepared to suit a specific application. All these formulations require the use of a surface active agent or surfactant, which is not only essential for its preparation and maintenance of long-term physical stability, but also to enhance biological performance of the agrochemical. Most active ingredient used in agrochemical formulation are water-insoluble compounds. The obvious reason for adding surfactants is to enable the spray solution to adhere to the target surface, and spread over it to cover a large area. In addition, the surface active agent plays a very important role in the optimization of the biological efficacy. The surfactants commonly used in adjuvants illustrate the wide array of surfactant chemistry available which includes anionic, nonionic, amphoteric and cationic surfactants; all can be found in today's adjuvant market. Generally some solvent or glycol can also present to hold the composition in a homogeneous state or control viscosity. Increasingly, if a solvent is essential it will have a high flash point and low vapour pressure since the practice of using isopropanol, acetone, or other flammable materials in adjuvant formulations is quickly disappearing due to the dangers of low flash point products. Other components common to adjuvants depending on type include oils (based on natural raw materials and petrochemical), gums and/or polymers, and oleochemicals like fatty acids or glycerin.

Adjuvants usually have multiple functions in relation to pesticide efficacy (Green and Beestman 2007). Increasing the foliar uptake of active ingredients is of particular importance for herbicides, growth regulators, and defoliants (Fig. 7.1). Therefore, the choice of the adjuvant in an agrochemical formulation is crucial (Tadros 2005).

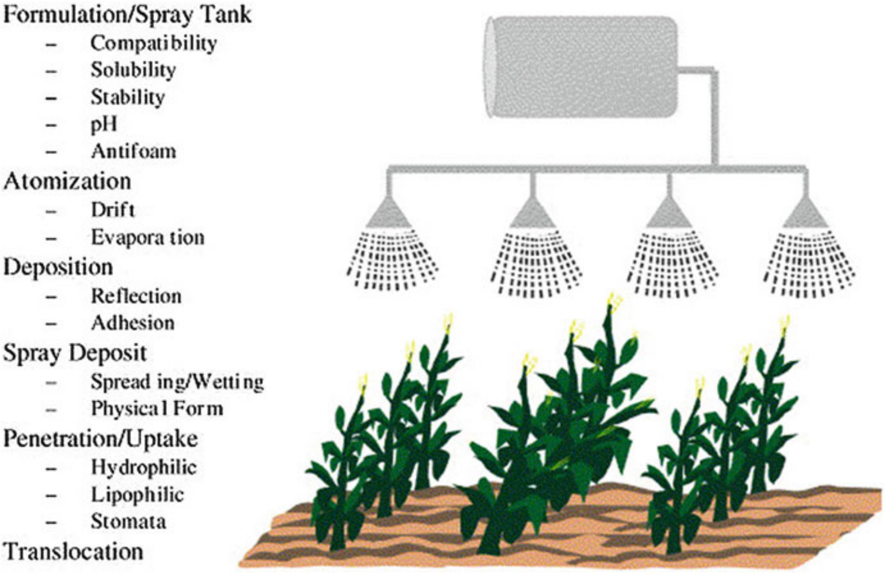


Fig. 7.1 Influence of formulation and adjuvants on herbicide performance (Reprint from Green and Beestman (2007))

It is actually difficult to ignore adjuvants when dealing with foliar uptake of pesticides. Indeed, the use of adjuvants dated back as early as about 200 years ago, although most of the synthetic adjuvant products started to emerge only a few decades ago.

Adjuvants are fascinating compounds. Typically showing no biological activity at all on their own, they help to exploit the full biological potential of many active ingredients. They can be absolutely necessary for some actives or to preserve activity, for example, under unfavorable environmental conditions or adverse water quality. Sometimes their mode of action appears obscure, since for a single active many different adjuvants with completely different modes of action, and used at differing rates per hectare, increase performance similarly. The other quite common extremes are situations where a particular adjuvant fits best to a particular active at a particular ratio in a particular formulation type, or conversely, where adjuvants are antagonistic to the product performance. In the case of adjuvants that somehow improve coverage, the visible mode of action correlates often with the achieved gain in performance.

However, most adjuvant effects are not visible at all since they occur at the molecular level, are time dependent and are often variable, since the adjuvant effects are based on interactions with the biological target and environmental factors. There are several good reasons to predict that adjuvant innovations will become even more important in the future.

The variety of products and technologies in the agricultural adjuvant industry has grown with the need to maximize the performance of pesticide products. These products have been shown to improve the performance of pesticides through aiding on-target delivery, maximizing efficacy of the active ingredient and improving spray water quality just to mention a few general areas of use. Development of pesticide formulations can be a rigorous science with the competing demands of maximizing performance of the active ingredient, maximizing the physical stability of the formulation, ensuring the human health and environmental effects of the formulation are minimized. Meanwhile, the costs of the product have to keep low enough so it makes business sense to bring it to market and for the customer to have value from its use. All of these factors must be balanced and can only be balanced by a team approach to developing the product.

Climate changes are likely to occur and possibly become more pronounced in the next decades. Weather is becoming more variable and drought spells will increase in many regions. Challenges for crop production are thus to increase crop productivity further considering that drought is only but one of the adverse conditions which crop production is already facing. Others include e.g. soil compaction, salinity, acidity or alkaline conditions, nutrient fixation or depletion. All those conditions interfere as well with the nutrient uptake of crops from soil. The development of new surfactant based-system as bio-activator for actives is a key factor to improve the cost-effective performance increasing process efficiency, energy and raw material savings. On the other hand, sustainability should take into account the use of renewable resources and the improvement of eco-friendly product profile.

7.2 Generic Pesticides of Growing Interest

Agrochemicals are an aging industry. While over 800 pesticide active ingredients remain on the market, the number of new substances being developed has fallen considerably over the last 10 years. In some industrialized country markets older products are losing their registrations. For example, the European Union review has removed over 360 active ingredients to date. But these and many other chemicals are still available elsewhere.

The overall global agrochemical pesticide market was valued at US$32 billion in 2004 with generic products making up an increasing percentage of this market. Latest estimates indicate that generic products account for US$18 billion, or around 66 % of overall sales and by volume, generic active ingredients may account for approximately 95 % of all product sales worldwide.

The types of generic most sold are herbicides with 57 % of the market, followed by insecticides with 34 % and then fungicides with 11 % of sales. The biggest selling generic is glyphosate with annual sales approximating US$5 billion followed by the insecticide imidacloprid with annual sales of around US$1 billion. The biggest selling fungicide is mancozeb, seventeenth in the list with sales of $220 million (see Table 7.1). On the other hand, generic active ingredients glyphosate, chlorpyrifos and cypermethrin, are produced by between 31 and 39 manufacturers.

Table 7.1 Market profile of the top 24 generic active ingredients (Adapted from Agrow's Complete guide to generic pesticides. Volume 2, Products and Markets (DS250), August 2005, pp 22–23)

Rank	Active ingredient	Activity	Value sales Sales ($m)	Prospects
1	Glyphosate	Herbicide	5000	Rising
2	Imidacloprid	Insecticide	1000	Rising
3	Malathion	Insecticide	400	Stable
4	Paraquat	Herbicide	400	Falling
5	Acephate	Insecticide	350	Rising
6	Pendimethalin	Herbicide	350	Stable
7	2,4-D	Herbicide	335	Stable
8	Acetochlor	Herbicide	300	Rising
9	Chlorpyrifos	Insecticide	300	Falling
10	Trifluralin	Herbicide	300	Stable
11	Atrazine	Herbicide	280	Stable
12	Imazethapyr	Herbicide	280	Falling
13	Lambda-cyhalothrin	Insecticide	275	Rising
14	Permethrin	Insecticide	270	Falling
15	Carbofuran	Insecticide	250	Falling
16	Deltamethrin	Insecticide	250	Stable
17	Mancozeb	Fungicide	220	Rising
18	Delta-cypermethrin	Insecticide	200	Rising
19	Carbendazim	Fungicide	200	Stable
20	Chlorothalonil	Fungicide	200	Stable
21	Cypermethrin	Insecticide	200	Rising
22	Dichlorvos	Insecticide	200	Falling
23	Linuron	Herbicide	200	Falling
24	Methomyl	Insecticide	200	Stable

7.3 Adjuvant Classification, Functionality and Chemistry

Although the first recorded use of adjuvants to increase herbicide performance was in the late 1890s, it was not until after the discovery of effective organic herbicides like 2,4-D in the 1940s that significant adjuvant research began (Foy 1989).

Adjuvants are defined as "an ingredient in the pesticide prescription, which aids or modifies the action of the principal ingredient" (Foy 1987). Adjuvants can be divided into two general types: (1) formulation adjuvants and (2) spray adjuvants. The first type consists of adjuvants, which are part of the formulation, while the second type of adjuvants is added along with the formulated product to the water in the tank of the spray equipment before application on the fields. Spray adjuvants are sometimes called tank mixing additives or just adjuvants, whereas the formulation adjuvants are called additives or inerts (Hochberg 1996).

The term adjuvant has developed several meanings in the agrochemical industry. In some parts of the world, adjuvant can refer to anything other than the pesticide formulation which is added to the spray tank. In other parts of the world, the term adjuvant is used interchangeably with the term formulant and refers to

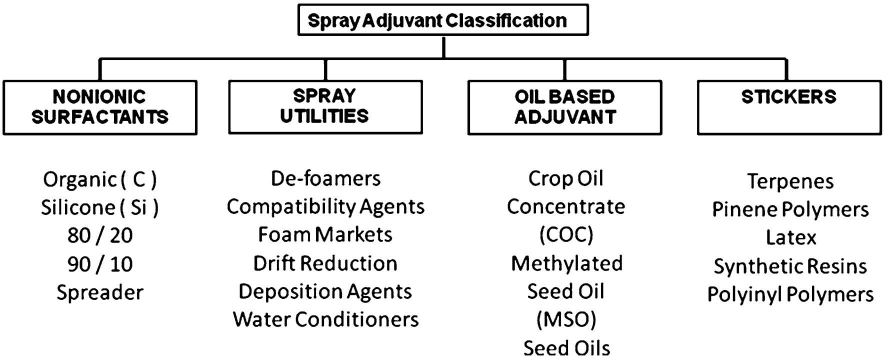


Fig. 7.2 Classification of adjuvants by tank mix function (Adapted from Roberts 2010)

any nonpesticidal ingredient in the formulated pest control product. Adjuvant terminology globally became such a large issue in the 1990s that several trade organizations decided to attempt standardizing both, the terminology and functionality of adjuvants.

Although several authors attempted to write materials for adjuvant terminology, only ASTM International (formerly American Society of Testing and Material) began to work on definitions for standard terms. ASTM E 1519 defines an adjuvant as a material added to a tank mix to aid or modify the action of an agrochemical, or the physical characteristics of the mixture (ASTM E 1519).

Although ASTM definitions are widely used, in some cases different terminology is adapted for unique circumstances. In 2009 the US Environmental Protection Agency (U.S. EPA) announced it was considering requiring the submission of residue data for active ingredients including an adjuvant as part of spray treatment when a spray tank adjuvant was included on the labelling. In order to facilitate EPA's investigation, industry proposed a set of classifications for tank mix adjuvants to minimize the testing necessary to provide the residue data EPA suggested it needed to establish a tolerance on food. The Spray Classification system presented to EPA utilized the ASTM definitions but aggregated specific adjuvants by broad type as a more general level of classification. Figure 7.2 illustrates the proposed classification of tank mix adjuvants (Roberts 2010).

The functions of adjuvants selected for use in tank mixtures vary widely depending on the needs of the active ingredient with which the product is applied. For example, certain active ingredients show enhanced performance from improved wetting while others may show enhanced performance from water conditioning or drift reduction. In some cases, the presence of an oil adjuvant may improve penetration and uptake of the active ingredient. A list of common crop protection products which respond to the use of a spray tank adjuvant along with the possible function provided by the adjuvant appear in Table 7.2 (Roberts 2010).

We have considered in the present review the term adjuvants to refer to any non-active ingredient in the formulated pest control product added to aid or modify the action of an agrochemical.

Table 7.2 Crop protection product combinations with spray tank adjuvants (Adapted from Roberts 2010)

Crop protection product	Desired adjuvant functionality
Glyphosate	Wetting, water conditioning
Sethoxydim	Cuticular penetration
Atrazine (post use)	Wetting, compatibility
Paraquat	Wetting, sticker
Glufosinate	Wetting, penetration, water conditioning
Imazapyr	Cuticular penetration
Acifluorfen	Wetting, cuticular penetration
Sulfonyl urea	Wetting, pH buffering
Fluazifop	Wetting, cuticular penetration
Pyraclostrobin	Cuticular penetration

7.4 Types of Surfactants

Surface-active agents have a characteristic molecular structure consisting on a structural group that has a very little attraction for water, known as a hydrophobic group, together with a group that has strong attraction for water, called hydrophilic group. This is known as an amphiphilic structure. The hydrophobic group is usually a long-chain hydrocarbon, and the hydrophilic group is an ionic or highly polar group. According to the nature of the hydrophilic group, surfactants are classified as: anionic, cationic, nonionic and amphoteric (Fernández Cirelli et al. 2008).

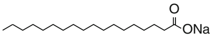
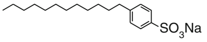
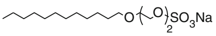
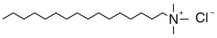
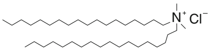
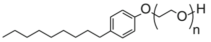
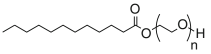
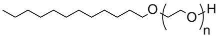
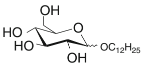
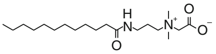
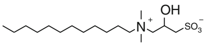
7.4.1 Anionic Surfactants

The hydrophilic groups of anionic surfactants consist in most cases of sulfonate, sulfate, or carboxylate groups with either a sodium or a calcium a counterion (Table 7.3). Amongst them, linear alkylbenzene sulfonate (LAS) are produced in the largest quantities worldwide. These are mainly used in powdery and liquid laundry detergents and household cleaners. It is important to point out that calcium linear alkylbenzenesulfonate is employed as adjuvant in many agrochemicals formulations.

7.4.2 Nonionic Surfactants

The hydrophilic behavior of nonionic surfactants is caused by polymerized glycol ether or glucose units (Table 7.3) (Fernández Cirelli et al. 2008). They are almost

Table 7.3 General classification and characteristic features of surfactants

	Alkyl tail	Polar head	Example
Anionic	C_8-C_{20} linear or branched-chain	–COOH	 Soap
	C_8-C_{15} alkylbenzene residues	$-SO_3Na$	 LAS
	C_8-C_{20} linear-chain ethoxylated	$-OSO_3Na$	 LES
Cationic	C_8-C_{18} linear-chain	$-N(CH_3)_3Cl$	 CTAC
	C_8-C_{18} linear-chain	$-N(CH_3)_2Cl$	 DODAC
Non-ionic	C_8-C_9 alkylphenol residues	$-(CH_2CH_2O)_n-OH$ n: 4–22	 APEO
	C_8-C_{20} linear or branched-chain	$-COO(CH_2CH_2O)_n-OH$ n: 4–22	 FAEO
	C_8-C_{20} linear or branched-chain	$-(CH_2CH_2O)_n-OH$ n: 2–22	 AEO
	C_8-C_{20} linear or branched-chain	$-NH(CH_2CH_2O)_n-OH$ n: 2–22	
	C_8-C_{20} linear or branched-chain	Glucose	 APG
Amphoteric	C_{10}-C_{16} amido-propylamine residue	$-N^{+}(CH_2)_2CH_2COO^{-}$	 (CAPB)
	C_8-C_{18} linear-chain	$-N^{+}(CH_2)_2CH_2CH(OH)CH_2SO_3^{-}$	 (CAHS)

exclusively synthesized by addition of ethylene oxide or propylene oxide to alkylphenols, fatty alcohols, fatty acids, fatty amines or fatty acid amides. Nonionic surfactants found major applications as detergents, emulsifiers, wetting agents, and dispersing agents. They are used in many sectors, including household, industrial and institutional cleaning products, textile processing, pulp and paper processing, emulsion polymerization, paints, coatings, and agrochemicals. A large amount of them are employed as adjuvant in many agrochemicals formulations.

7.4.3 Cationic Surfactants

Cationic surfactants contain quaternary ammonium ions as their hydrophilic parts (Table 7.3). This class of surfactants has gained importance because of its bacteriostatic properties. Therefore, cationic surfactants are applied as disinfectants and antiseptic components in personal care products and medicine. Because of their high adsorptivity to a wide variety of surfaces, they are used as antistatic agents, textile softeners, corrosion inhibitors, and flotation agents.

7.4.4 Amphoteric Surfactants

Amphoteric surfactants containing both cationic and anionic group in their structure and sometimes are referred to as zwitterionic molecules (Table 7.3). They are soluble in water and show excellent compatibility with other surfactants, forming mixed micelles. The change in charge with pH of amphoteric surfactants affects wetting, detergency, foaming, etc. The properties of amphoteric surfactants resemble those of non-ionics very closely. Zwitterionic surfactants have excellent dermatological properties, they also exhibit low eye irritation and are frequently used in shampoos and other personal care products. Amphoteric surfactants are now starting to be used in agrochemicals formulation.

7.5 Mode of Action of Adjuvants

Despite the negative perception of the public, pesticides are still going to be used for many decades to ensure the food supply for the ever growing world population. The simple reason for this is that products more costly for farmers mean more expensive foods for the population, alternative methods for plant protection are either inefficient or too costly for farmers.

The global pesticide production in 2000 amounted to over 3 million tons of active ingredients (Tilman et al. 2002). It is estimated that of the total amount of pesticides applied for weed and pest control, only a very small part (<0.1 %) actually reaches the sites of action, with the larger proportion being lost *via* spray drift, off-target deposition, run-off, photodegradation and so on (Pimentel 1995). Agrochemical industries are continuously seeking for new products and formulations of expanding area of use and market share. It typically takes at least 10 years of intense research and development from the discovery of an active ingredient until its market introduction as an agrochemical product (Cordiner 2004). In addition, it has become increasingly more and more difficult to find materials of high activity that are environmentally friendly, safe and cheaper to manufacture. Most government and regulatory authorities are now demanding formulations that are cleaner and safer for the users, have minimal impact on the environment, and can be applied at the lowest dose rate (Holden 1992).

The transporting-limiting barrier restricts the performance of foliar-applied agrochemicals molecules such as pesticides, fruit chemical thinning, and growth regulators (Schreiber 2006; Petracek et al. 1998). An agrochemical active ingredient is often ineffective and of little use to the end user if applied to the target surface alone (Tominack 2000). In most cases the active ingredient is formulated into complex, carefully designed multi-agent preparations that facilitate mixing, dilution, application and stability. To enhance the efficacy of foliar-applied agrochemicals, surfactants are widely used in spray solution to increase active ingredient solubility, to improve wetting of the plant cuticle, and to increase cuticular penetration.

Around 230,000 t of surfactants is used annually in agrochemical products, with a formulation typically containing 1–10 % of one or more surfactants (Edser 2007). Surfactant, as a plasticizer, softens the crystalline waxes in cuticle and thus increases the mobility of the agrochemicals across the cuticular membrane (Schönherr et al. 2000).

With the presence of surfactant, the sorption behavior of plant cuticle becomes very complex. Derived from similar studies, surfactant demonstrates two opposite effects on the cuticle sorption behavior: (i) surfactant solutions decrease the distribution of organic contaminant onto the cuticle by increasing the solute aqueous solubility, that is, a negative effect; (ii) surfactants increase the sorption capability by softening of cuticular wax (i.e., plasticizing effect) or by forming a new partition phase for the cuticle-sorbed surfactant, that is, a positive effect (Zhu et al. 2004; Lee et al. 2000, 2004). The apparent effects of surfactants on sorption depend on the balance of the two opposite effects, which are dominated by the compositional characteristics of plant cuticles, surfactant type and concentration, and the solute's properties (Tamura 2001).

On the other hand, it is well known that droplets of between 50 and 250 mm diameter will adhere to plant surfaces, but larger droplets may rebound or shatter (Hartley and Brunskill 1958). However, smaller droplets are more prone to drift, so we have the classic conundrum of how to achieve maximum on-target adhesion/retention, with minimum off-site drift. The exact mechanism by which these molecules elicit this acceleration of movement is not yet fully understood.

In the case of systemic pesticides, if there is little or no uptake, then regardless of the efficiency of deposition and retention, this will have been to no avail. Obviously environmental factors, such as rain (causing wash-off), wind and relative humidity (affecting droplet drying), will materially affect pesticide uptake. However, a major factor in all cases is the plant leaf itself, including its surface and cuticle. One of the main functions of spray adjuvants is to overcome or minimise the effect of leaf waxes and the cuticular barrier. Appropriate adjuvants will substantially aid droplet spread, redistribution and leaf coverage, but can also enhance uptake of the active ingredient. Penetration and absorption of a compound by leaves is determined by the ability of the compound to move through the cuticle, a process known as transcuticular penetration or movement (Solel and Edgington 1973).

Foliar uptake of pesticides is a diffusion process across the epicuticular wax, the cuticle, and the plasma membrane of epidermal cells. The diffusion rate of both lipophilic and hydrophilic compounds across isolated leaf cuticles was negatively correlated with their molecular weight (MW), or molecular size (Bauer and Schönherr 1992; Schönherr and Schreiber 2004). In fact, the plasmodesmata of plants can only allow free circulation of molecules smaller than 1 kDa (Oparka and Roberts 2001). It is thus not a coincidence that most foliar-applied herbicides have a molecular weight between 100 and 500, as any out-ranged molecules would be eliminated at the screening stage if they cannot enter plant leaves or move between cells (Tice 2001).

Lipophilicity is probably the single most important property of pesticides related to foliar uptake. Generally, an octanol/water partition coefficient (log Ko/w or log$P$)

is used to describe the lipophilicity of a compound. Chemicals with log $P < 0$ are considered as hydrophilic and those with log $P > 0$ lipophilic. Due to the lipoidal nature of the epicuticular wax and the cuticle, foliar uptake tends to increase with increasing lipophilicity of the chemicals (Baker et al. 1992; Stevens et al. 1988). A best example showing this is the faster uptake of 2,4-D ester (lipophilic) compared to 2,4-D salt (hydrophilic) (De Ruiter et al. 1993).

However, like molecular size, log$P$ is not the only property that determines the foliar penetration. Indeed, based on the uptake data obtained with 26 chemicals and four plant species, only a moderate correlation ($R2$: 24–45 %) was found between log$P$ and the foliar uptake of chemicals. In fact, some hydrophilic compounds, such as paraquat, are actually able to penetrate into plant leaves very fast.

7.6 Plants Cells Morphology

Plant cells, unlike animal cells, are surrounded by thick walls that form rigid tissues. They do not need the junctions found in animal tissues. But some higher plant cells are interconnected by plasmodesmata, tubelike structures that penetrate through cell walls and form fluid connections between adjacent cells. Like gap junctions in animal cells, plasmodesmata allow the free exchange of small molecules and help coordinate the activities of neighboring cells.

On the surface of the leaves of higher plants is a layer of waxy material known as the cuticle or cuticular membrane (Kirkwood 1999; Riederer and Schreiber 2001). It is theorized that after plants migrated from the sea onto land 400 million years ago, in the Silurian period of the Paleozoic era, cuticles evolved as a means of reducing water loss to the surrounding air (Stewart et al. 1993; Thomas and Spicer 1987). The plant cuticle is a thin continuous layer of predominantly lipid material synthesized by the epidermal cells and deposited on their outer. Cuticle composition and structure of modern higher plants vary greatly from species to species but are generally 0.1–10 μm thick, being composed of two major classes of lipids: (i) solid waxes, usually mixes of long chain aliphatic compounds and (ii) insoluble, high molecular weight polyester cutins. Plant cuticle contains too terpenoids and phenolic compounds, some of which serve as anti-feedants to discourage grazing by herbivores.

There are five basic types of cuticles: smooth, ridged, papillose, glaucous (having an additional covering of microcrystalline wax), and glandular where trichomes are present in high number and comprise the main surface of the leaf (Hess and Foy 2000).

Generally, the plant cuticle is composed of two regions. The lower region consists of cutin, long chain alkyl ketones, alcohols, and closest to the cells, polysaccharides; the upper region consists of epicuticular wax, mostly very long chain alkanes (Li and Chen 2009; Chen et al. 2008).

The epicuticular wax present in the outer surface of the membrane has two main forms, crystalline and amorphous (Jeffree 1996; Chen and Li 2007). Whereas there are some important exceptions, the dominant epicuticular wax on leaves of grass species is crystalline and on broadleaf species is amorphous. The crystalline wax is undoubtedly an obstacle for spray retention and an intimate contact between pesticide droplets and leaf surface, but it does not seem to be a formidable barrier for pesticide uptake. All aerial surfaces of plants are covered by the cuticle. It is widely known that the waxy sheet of cuticle not only prevents water loss, but also functions in defense by forming a barrier that resists physical damage and microbial invasion. The cuticle is incontestably the most important barrier for the penetration of pesticides. The microscopic structure and chemical composition of plant cuticles were reviewed by Holloway (Holloway 1993).

The cuticle permeability for pesticide molecules varies greatly with plant species and growth stage, but is not correlated to the thickness (Becker et al. 1986; Buchholz et al. 1998). It is clear that both lipophilic and hydrophilic compounds can diffuse through the cuticle. It was postulated that lipophilic and hydrophilic chemicals follow distinct pathways, i.e., polar (aqueous pores) and apolar (cutin matrix and wax) routes (Crafts 1960). Until now the existence of aqueous pores inside the cuticle is only supported by indirect evidence obtained through studying the diffusion characters of calcium salts and glyphosate across isolated leaf cuticles (Schönherr 2000, 2002).

Their high sorption capability may be seriously suppressed and even inhibited by the cuticular waxes deposited within and on the surface of the polyester matrix because of their partially cristaline structure. More importantly, it is the arrangement of the wax into amorphous and crystalline domains that is believed to be the transport limiting barrier (Reynhardt and Riederer 1994; Santier and Chamel 1998). Removal of waxes from bulk plant cuticles promotes their sorption capability and leads to an increase in the permeability by several orders of magnitude (Chefetz 2003; Popp et al. 2005).

7.7 Mechanism of Action of Adjuvants

It is generally recognized that not any surfactant can increase the uptake of any herbicide. At present, there is no practical theory or comprehensive model that can predict quantitatively the effect of a particular surfactant on the uptake of a specific herbicide. Applying the right concentration and type of surfactant is not an easy task for the user. Systematic studies will be needed to elucidate the mechanisms involved in the complex interactions between herbicides, surfactants and plants. In order to improve the uptake of post-emergence herbicides, numerous surfactants have been tested over the last 30 years. However, until the early 1990s, most experiments involved only a few randomly selected surfactants and it was not possible to know which parameter of surfactants was most important for enhancing herbicide uptake.

A first review of the mechanisms of action is listing various contributions like wetting and spreading, dissolution or disruption of epicuticular waxes, solubilisation of agrochemicals in deposits, prevention or delay of crystal formation in deposits, retention of moisture in deposits by humectant action, and promotion of uptake of solutions via stomatal infiltration (Stock and Holloway 1993).

A first mechanistic approach of the adjuvant/wax interactions was reported by Schreiber (Schreiber 1995). From the observation that the surfactant-induced acceleration of the diffusion of pentachlorophenol is completely reversible if the surfactant is removed, it was tentatively concluded that the effect of the surfactant on wax is an unspecific plasticising interaction. It was not before a decade later that again a plasticising effect was revealed from macro and micro-thermal analysis of plant/surfactant interactions (Perkins et al. 2005). Finally, a series of results from different experiments with reconstituted cuticular wax, like the already mentioned reversibility of diffusion rates when adjuvants are removed, like the decrease in size selectivity in the presence of adjuvants, and like the fluidity increase in the presence of adjuvants as determined by electron spin resonance (ESR) and by nuclear magnetic resonance (NMR), clearly allow the conclusion that the adjuvants act by a non-specific, plasticizing mechanism (Schreiber 2006; Petracek et al. 1998).

An even deeper insight into the uptake-enhancing mechanism of adjuvants is reported by Burghardt et al. (Burghardt et al. 1998). In this paper, a free volume model was applied to predict diffusion coefficients of active ingredients on the basis of the transport properties of the wax, the molar volume of the diffusing compound and the adjuvant concentration in the wax. Increase in the mean free volume by the plasticising action of adjuvants raises the probability for a diffusing compound to find a fitting void. Despite these experimental and theoretical advances, it was stated by Wang et al. that a more multidisciplinary approach is needed to elucidate the transcuticular diffusion behaviour of active ingredients and the mode of action of adjuvants (Wang and Liu 2007).

7.8 Efficiency Parameters to Increase the Agrochemicals Performance

7.8.1 Cuticular Uptake

One of the most important ways to improve the efficacy of pesticides and minimize their impact on off-target organisms is through increasing the penetration of active ingredients into plant foliage. If foliar uptake is important for the efficacy of systemic fungicides and insecticides, then diffusion into plant tissues is a prerequisite for the activity of foliar-applied herbicides, growth regulators, and defoliants. Foliar uptake of pesticides is a complex process, depending on leaf surface characters of plants, physicochemical properties of the chemicals, types and concentration of the additives, and environmental conditions. How each of these factors influences the uptake is only partially understood, despite an urgent demand for efficient use of pesticides.

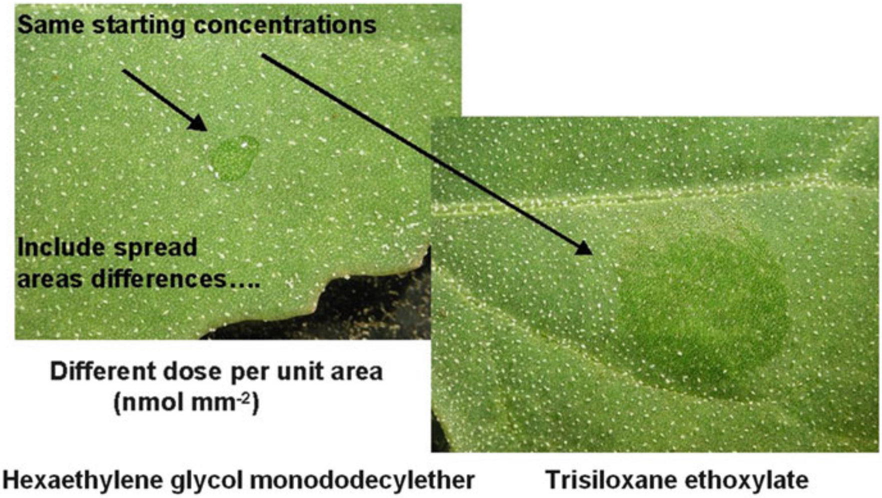


Fig. 7.3 Illustration of droplets spread effects on *Chenopodium album* with different spray formulation (Reprint from Zabkiewicz (2007))

Cuticular uptake (diffusion of the chemical directly through the cuticle) of pesticides has been studied for a longer time, but progress in understanding the factors controlling this mechanism has been much slower. Attention was focussed on relating the physical properties of the formulation to percentage uptake, with less focus on the interactions of adjuvant(s) in a spray formulation, or the importance of plant cuticle and epidermal layers (Stevens and Bukovac 1987; Stock et al. 1993). Just as it is essential to consider application and formulation together in the case of adhesion and retention by plants, so the interactions of plant, active and adjuvant must all be considered in the uptake process.

The fundamental mechanism of uptake has been considered, with most attention given to the epicuticular lipids and their role in modifying active ingredient diffusion through cuticles (Kirkwood 1999; Riederer and Markstädter 1996; Schönherr et al. 1999). However, there is a much simpler effect on the leaf surface that needs to be considered first. If a spray formulation contains adjuvants that cause droplet spread on a leaf surface (Fig. 7.3), this will in effect lower the mass of active per unit area, and without any change in concentration until the spray solution begins to evaporate. In any case, there will be a “solution residue”, where the concentration of the active is many times more than in the starting spray solution (Zabkiewicz 2003).

7.8.2 Translocation

Absorption and translocation of herbicides can be significantly increased when adjuvants are added to foliar applied spray mixtures level of increased control from

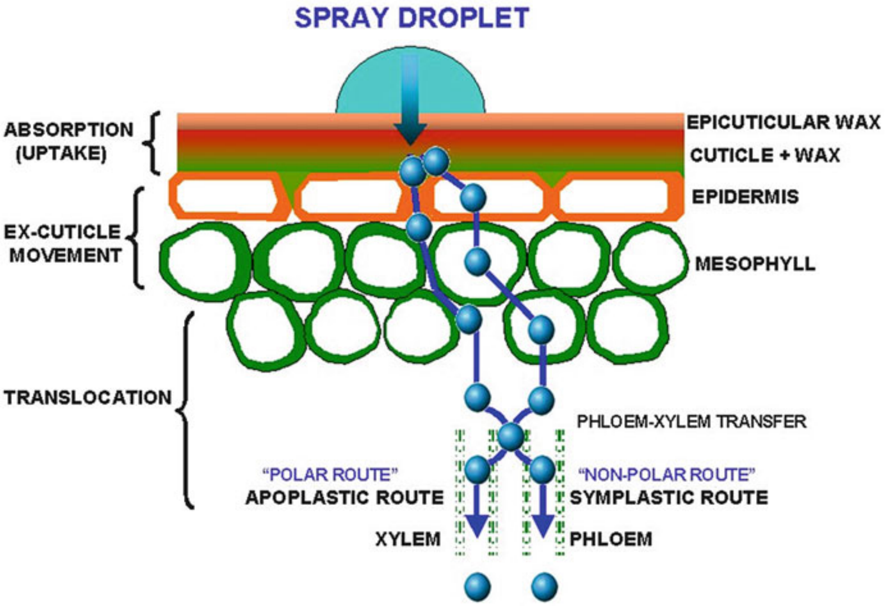


Fig. 7.4 Representation of different trans-cuticular pathways and subsequent apoplastic (*polar*) and symplastic (*non-polar*) pathways (Reprint from Zabkiewicz (2007))

adjuvants is usually affected by the environmental conditions at the time of herbicide application. In most cases, herbicide absorption and translocation are greatest under environmental conditions which are most favorable for growth of the treated plant. Adjuvants added to treatment solutions often increase absorption and translocation of foliar applied herbicides, especially when plants are under stress at time of treatment (Wills and McWhorter 1988).

Translocation has received the least attention, though long distance transport has been well studied and reviewed (Price 1976; Coupland 1988). In the case of foliar applied pesticides, it is known that lipophilicity is important, as these compounds have to cross hydrophobic membranes or structures other than the cuticle proper. Hydrophilic molecules are readily transported in either the phloem (downwards) or the xylem (upwards), though their initial movements through the cuticle, epidermal cells and into the mesophyll are not well understood (Devine and Hall 1990). The presence of separate "hydrophilic" and "lipophilic" pathways as part of the uptake process, may in turn determine the efficiency of the subsequent translocation pathway, but it is also difficult to define when uptake becomes translocation (Fig. 7.4).

Practically all herbicides and all systemic pesticides are weak electrolytes. Bromilow et al. (1990) represented polarity or lipophilicity and acid strength (pKa), as two main herbicide characteristics that help in understanding the transport pattern in plants. As the chemicals become more polar and more lipophilic, the permeation rate decreases. The pH in the exterior of the cell is approximately 5.5, herbicides

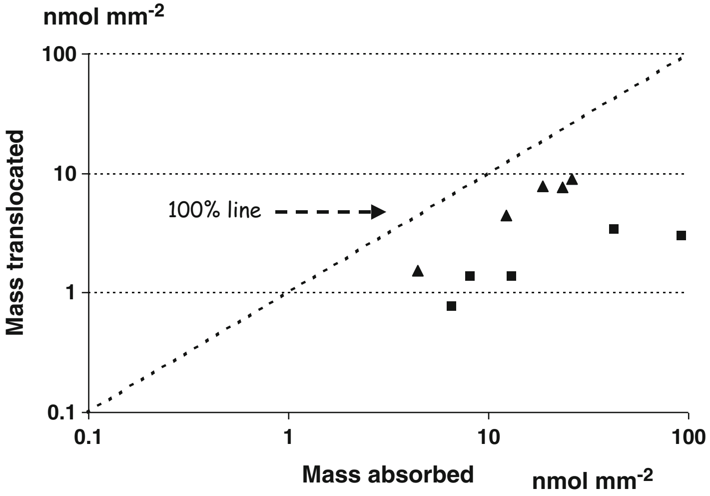


Fig. 7.5 Glyphosate mass uptake into *Chenopodium album* versus mass absorbed from Roundup® Ultra (▲) and Touchdown (■) commercial formulations; (- - -) maximum uptake line, representing 100 % uptake over the initial dose range (Reprint from Zabkiewicz (2007))

with pKa below 5.5 are in a non-dissociated form and are thus able to penetrate the cell more easily. Once at the cytoplasm, where the medium is more alkaline (pH approximately 7.5), these herbicides disassociate and turn into the most active, and less capable, translocating form of the molecule. Because the dissociated form is less capable of spreading to the exterior of the cell, the molecules of these herbicides get "stuck" in the cytoplasm; this behavior receives the name "ionic trap". In addition, plasmodesmata may have significant participation in translocation of molecules that have pKa (dissociation constant) below the pH of the xylem, which is approximately 5.5; it may also assist symplastic movement of these molecules by other routes besides phloem (Trapp 2004).

It is clear that "long-term" translocation will be affected by plant growth stage and environmental conditions, but "short-term" translocation (over hours rather than days) may have other rate limiting or modifying features.

Adjuvants are known to facilitate cuticular "transport" (foliar uptake) but are not thought to play any significant part in further short or long-distance translocation processes. However, in theory, if adjuvants could reach the cellular plasmalemma, then they could affect the initial stage of the sub-cuticular transport process (Fig. 7.4). The recent use of mass or molar relationships, instead of percentages, for xenobiotic uptake into plants from differing formulations, may be a means of elucidating some of the interactions among actives, adjuvants and plants (Forster et al. 2004).

It has been demonstrated that a relationship similar to that developed for mass uptake, for translocation vs. mass absorbed (which is related to the initial dose applied) can also apply to the translocation process in model systems but less well with complex formulations (Fig. 7.5) (Zabkiewicz 2007). For example, the commercial glyphosate formulations show considerable interaction, if the reduction in both mass uptake and translocation at higher initial dosages, is a correct indication. This manner of presenting mass uptake and translocation has the potential to identify anomalous behaviour or complex interactions.

The advantage of the mass relationship is that it can provide information similar to that used for drug delivery dose prescriptions. Knowing the mass uptake, an estimation can be made of the mass translocated in specific systems; with subsequent studies on the influence of physiological and environmental influences, appropriate "dosages" could be applied at specific growth stages or conditions. It can also be used to estimate the change in overall efficacy of spray formulations, as to date no generic quantitative relationship has been identified.

The principal factors controlling foliar uptake appear to be solute mobility in the cuticle, cuticle tortuosity and solute-driving force.

7.8.3 Environmental Conditions

It is well known that environmental conditions have an important influence on herbicide efficacy. In particular, the effect of humidity on herbicide uptake has been attributed to changes in cuticle hydration and droplet drying. As early as the 1950s, it was hypothesized that humectants such as glycerol would enhance herbicide uptake by not letting droplets dry, thus maintaining the herbicide in solution, and hence making it available for uptake. Shortly thereafter, evidence was found to support this hypothesis and humectants were used successfully in warm, dry areas to increase herbicide efficacy. Furthermore, current evidence suggests that highly water-soluble, ionic herbicides may be more sensitive to low humidity and rapid drop drying than lipophilic herbicides. The interaction of water-soluble herbicides with surfactants, the cuticle, and humidity, with particular emphasis on the impact of low humidity and humectants on herbicide uptake is presented by Ramsey et al. 2005. It was found that when one focuses on research performed at low humidity the importance of humectants emerges, which is not in keeping with what is now commonly accepted (Ramsey et al. 2005).

It is well known that the activity of foliar-herbicide sprays is influenced by the environmental conditions at the time of spraying. Current evidence suggests that water-soluble herbicides may be more sensitive to variations in spray conditions than lipophilic herbicides.

Among the many environmental factors that can affect herbicide uptake, two of the most important are temperature and humidity, with optimal uptake being favoured by warm, humid conditions (Muzik 1976).

Temperature can affect herbicide uptake by changing the viscosity of cuticle waxes, the rate of diffusion, and in conjunction with humidity, cuticle hydration (Price 1983). Increased diffusion of solutes into cuticles with increasing temperature has been explained as a result of lower partition coefficients (log P) as temperature increases (Schönherr et al. 1999).

By the mid-1980s, it appeared as though research on humectants gave way to investigations on the effect of ethylene oxide (EO) content on surfactant performance. Ethoxylated surfactants have been shown to be effective at increasing the uptake of both lipophilic and hydrophilic herbicides.

However, an important observation from research on ethoxylated surfactants is that for water-soluble herbicides, surfactants that increase droplet spreading often result in poor uptake compared to surfactants that are poor spreaders and have higher surface tension. The reason for this is unclear, but it may be related to the fact that droplets with high surface tension have smaller surface areas for evaporation than droplets with low surface tension, which disperse across the leaf surface (Zhu et al. 2008).

7.9 Agro-adjuvants Models

The traditional method of study and development of different formulations has been to conduct experimental trials (both field trials and controlled environment trials) which are time consuming, expensive, and product specific. More recently, models are being developed that take a more mechanistic approach to the different aspects of spray application with the hope of gaining insight into the underlying physical processes (Zabkiewicz 2000). Often these models consist of sub-models of individual aspects of interest. The challenge in the future is to bring these modeling approaches together in a coherent and systematic way so that an integrated formulation efficacy support system can be developed.

By their nature comprehensive detailed models have large numbers of parameters that tend to be plant and a.i. specific and may be difficult to determine. An example of such a comprehensive model is given by the series of papers by Satchivi et al. (2000a, b, 2001, 2006). The results from these types of models are usually excellent but care must be taken that they are not used outside of their limitations (Trapp 2004). By their very nature these comprehensive models include many competing mechanisms for active ingredient uptake. Due to this the effects of varying one parameter (say droplet size) is not always obvious. The benefit of simplified models, such as that presented here, is that results are not obscured by surfactant adjuvants (Tu et al. 2003). The precise nature of this increased foliar uptake is not well understood but hydrophilic compounds generally show larger increases in uptake than lipophilic ones (Stock et al. 1993). Initial dose per unit area has been shown to be a strong determinant of uptake for surfactants of various spread characteristics (Forster et al. 2004). The addition of a surfactant can lead to greater droplet spreading and so the dose per unit area is reduced but it is applied over a larger area. These phenomena were investigated to determine what effect an increased spread area has on uptake. To be able to model the effect of droplet size and spread area a model with both horizontal (along the leaf surface) and vertical (into the leaf) spatial dimensions are needed as well as time dependence. To simplify the analysis circular symmetry of the droplet is assumed so the along leaf dimension is simply

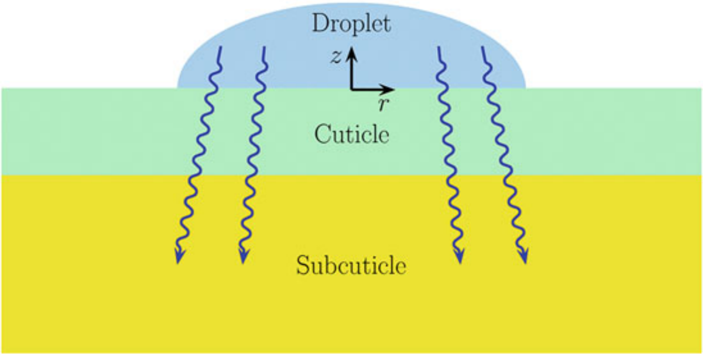


Fig. 7.6 The schematic of the layers used in the numerical solution (Reprint from Mercer (2007))

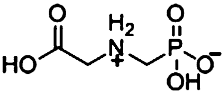


Fig. 7.7 Glyphosate structural formula

the radius from the centre of a circular droplet. A three layer model is used as shown in Fig. 7.6. The upper layer is the droplet, the middle layer the cuticle and the lower layer the subcuticle. The governing process is assumed to be a simple diffusion process with removal of active ingredient in the subcuticle region (Mercer 2007).

The effect spray droplet size and spread area have on the diffusion of a hydrophilic active ingredient through a leaf cuticle and therefore on its eventual uptake by the plant. The model presented here is not designed to be a comprehensive detailed model of all the physical processes involved but rather a simplified model so that specific size and area related factors can be investigated.

7.10 Toxicity of Adjuvants for Glyphosate

Toxicity of wetting agents employed in the formulations of glyphosate will be analyzed in this section, because glyphosate is the most important pesticide worldwide and the amount of wetting agent present in glyphosate formulation becomes as high as 150 g/lt.

Glyphosate, N-(phosphonomethyl)glycine, the active ingredient of very well-known herbicide preparations, such as Roundup®, is a systemic and non-selective herbicide utilized for weed control, i.e. in agriculture, forestry, urban areas and even aquaculture (Woodburn 2000; Williams et al. 2000).

The use of this non-selective and broad-spectrum herbicide increased dramatically after the introduction of genetically modified glyphosate-resistant crops in

1997 (Giesy et al. 2000). Although glyphosate is already one of the most used xenobiotics in modern agriculture, we should expect an increasing utilization of glyphosate largely due to the number of transgenic plants developed to be tolerant to this herbicide (May et al. 2002; Nadler-Hassar et al. 2004; Stephenson et al. 2004).

The main formulation of glyphosate is Roundup®, where glyphosate is present as an isopropylamine (IPA) salt and its efficiency is enhanced by addition of the surfactant polyoxyethylene amine (POEA) (Tsui and Chu 2003).

Virtually, every pesticide product contains ingredients other than those identified as the "active" ingredient(s), i.e. the one designed to provide the killing action. These ingredients are misleadingly called "inert". Commercial glyphosate formulations are more acutely toxic than pure glyphosate, since the amount of Roundup® required to kill rats is about 1/3 of the amount of glyphosate alone (Martinez and Brown 1991). Similar results have been obtained in cell division, thus indicating a synergy between glyphosate and Roundup® formulation products (Marc et al. 2002). There are in the literature important studies regarding the possible impact on environment and human health toxicity of glyphosate, particularly since there is a paucity of data regarding chronic exposure to sublethal doses during embryonic developments (Paganelli et al. 2010) but they have not included due to it is out of the scope of this review.

Moreover, regarding the herbicide commercial formulation, the negative impact of polyoxyethylene tallow amine (POEA) surfactant towards examined amphibians was emphasized as correlated with the pH value of water environment. This latter finding is well harmonized either with the literature data (Krogh et al. 2003). POEA represents the group of nonionic alkylamine ethoxylates (ANEOs), which have been employed in agrochemical formulations and as spray adjuvants since the 1970s of twentieth century. For many years these chemicals were treated as non-toxic biodegradable additives; however, over the past two decades the knowledge on their adverse impact, especially on aquatic biota, increased dramatically (Krogh et al. 2003).

The traditional glyphosate surfactant system (called MON 0818) is a blend of components that contains a complex polyethoxylated tallow-amine (POEA) surfactant mixture. The primary component of MON0818 is POEA surfactant (about 75 %) (Wan et al. 1989). The other 25 % of ingredients have been determined to be relatively non-toxic (LC50 > 100 mg l^{-1} for various ingredients to a variety of freshwater species; US Environmental Protection Agency ECOTOX Database), and therefore are unlikely to substantially contribute to the toxicity of MON 0818. The POEA surfactant component consists of a complex mixture of polyethoxylated long-chain aliphatic amines, which can be considered non-ionic in the neat form. In the aqueous environment of the microcosms used in the study, it is at least partially protonated and can be considered cationic.

Wade et al. reported that Mon 0818, a tallow amine surfactant, increased the diffusion of glyphosate into isolated plasma membrane vesicles, suggesting that surfactants could increase the membrane permeability (Wade et al. 1993).

On the other hand, the application of herbicides to control emergent aquatic vegetation or to treat the banks of waterways can produce localized concentrations of glyphosate and surfactant in water that are greater than those from runoff associated with terrestrial uses (e.g., associated with agriculture). Glyphosate has been shown to be slightly toxic or non-toxic to aquatic organisms, whereas the MON 0818 surfactant containing POEA is considered to be moderately toxic (Giesy et al. 2000). Some studies have noted that the concentrations of MON 0818 in shallow water could reach levels that present an elevated risk to aquatic organisms (Wan et al. 1989; Folmar et al. 1979; Servizi et al. 1987). The risk potential of MON 0818 in shallow water is a function of both toxicity and environmental fate. Although numerous studies have been conducted to evaluate the fate and toxicity of glyphosate, limited information is available on the fate and toxicity of the surfactant alone (Giesy et al. 2000; Wan et al. 1989; Folmar et al. 1979; Goldsborough and Brown 1993; Beyers 1995; Gardner and Grue 1996; Franz et al. 1997; Henry et al. 1994; Paveglio et al. 1996). The majority of information available on the environmental fate of non-ionic ethoxylated surfactants pertains to linear alcohol ethoxylates and alkylphenol ethoxylates, which dissipate in the aquatic environment through adsorption to sediment and biodegradation by microbial action (Krogh et al. 2003; Urano et al. 1984; Cano and Dorn 1996).

Since aquatic weed control can occur in relatively shallow water bodies containing various types of sediments, Wang et al. assessed changes in aqueous concentrations of MON 0818 and changes in its toxicity to the cladoceran *Daphnia magna* over time in microcosms with and without natural sediments (Wan et al. 1989). The toxicity of the POEA surfactant, MON 0818, decreased rapidly in water from microcosms containing sediment, and this decrease in toxicity was correlated with the decline of MON 0818 concentrations in the overlying water. These results indicate that toxicity and concentration of the surfactant can be rapidly reduced in shallow water due to interactions with sediments. Although the present study did not directly address the potential for chronic exposure of aquatic organisms to the POEA surfactant, the strong tendency for this surfactant to adsorb rapidly to sediment, together with biodegradation, suggest that risks of chronic toxicity would be low. Furthermore, it also appears that dissipation is increased in the presence of sediment containing higher percent clay and total organic carbon, and higher microbial mass. The information obtained from the chemical analyses and toxicity tests illustrates the utility of applying different approaches to understanding complex surfactant-related issues. The mechanism of dissipation is likely to be related to either sorption or microbial degradation of the POEA surfactant (Giesy et al. 2000).

On the other hand, the organic carbon partition coefficients (K_{oc}) of ^{14}C-labeled POEA surfactant in three different soil types (silt loam, silt clay loam, and sandy loam) ranged from 2,500 to 9,600, suggesting that the surfactant would strongly adsorb to soil (Marvel et al. 1974). In the present study, the POEA surfactant could rapidly adsorb to the surface of the sediment layer and to suspended sediment (a small amount of sediment was suspended into the water column when adding the MON 0818 solution into microcosms and when removing the sheets of aluminum foil from the surface of sediment at the beginning of the study). Microbial degradation can also contribute to the dissipation of POEA from natural water bodies. However, the rate and extent of degradation will depend on the types and amounts of microbes present in the water and sediment. While no study on the microbial degradation of POEA surfactant is available in a water–sediment system, a study using ^{14}C-labeled POEA surfactant in natural water containing suspended sediment reported a half-life of less than 3–4 weeks (Banduhn and Frazier 1978).

The half-lives of POEA surfactant reported by Banduhn and Frazier were obtained in a system of natural water and suspended sediment that likely had a relatively low microbial population (Banduhn and Frazier 1978). Using limited data, Giesy et al. estimated that the aquatic half-life for POEA surfactant would range from 21 to 42 d, which is substantially longer than the half-lives of 13 and 18 h that we estimated for shallow (12 cm) water columns in contact with sediments (Giesy et al. 2000). Sorption and degradation could be expected to occur in the presence of sediment.

Contardo-Jara et al. showed that glyphosate accumulates in L. variegatus, despite the hydrophilic character of the herbicide (Contardo-Jara et al. 2009). The accumulated amounts of glyphosate and the added surfactants in Roundup® Ultra cause an elevation of the biotransformation enzyme sGST at non-toxic concentrations and antioxidant enzyme superoxide dismutase was significantly increased by glyphosate but in particular by Roundup® exposure indicating oxidative stress. The accumulation and the enzymatic response of the worms were clearly higher in the animals exposed to Roundup®, indicating that the formulation Roundup® is of more ecotoxicological relevance than the glyphosate itself.

The alterations demonstrated by Peixoto[102] in mitochondrial bioenergetics caused by Roundup® cannot be exclusively attributed to the active ingredient, but may as well be the result of other chemicals e.g. POEA, or due the possible synergy between glyphosate and Roundup® formulation products (Peixoto 2005). This synergy between glyphosate and Roundup® inert ingredients has also been reported in cell division, where the delay observed in the cell cycle could be the result of alterations on the mitochondrial bioenergetic reactivity's, which have drastic consequences on cellular function through the perturbation of the bioenergetic charge and balance of the cell (Marc et al. 2002). Therefore, the reduced energetic efficiency of mitochondria may account for some toxic effects resulting from the impairment of the energy requirements of the cell and from the crucial importance of energy metabolism in active tissues, e.g. liver. Marc and co-workers found that the so called "inert ingredients" used in Roundup® are greatly responsible for the observed toxicity at the bioenergetic level. Data obtained in this study clearly demonstrate the ability of Roundup® to impair mitochondrial bioenergetic reactions. Alteration of basic mitochondrial functions was monitored by the detection of changes induced in mitochondrial respiration and membrane energization (Δ_ψ). Bearing in mind that mitochondria is provided with a variety of bioenergetic functions mandatory for the regulation of intracellular aerobic energy production and electrolyte homeostasis, these results question the safety of Roundup® on animal health.

7.11 Screening and Efficacy of New Surfactants for Glyphosate

Developing new plant protection formulations is a challenging task. The formulation of the active ingredient must assure a long shelf life stability including very high and low temperatures, a high loading and at the same time, the active ingredient needs to be optimal bioavailable. Greenhouse tests to evaluate the biological performance are regularly done with small plants and spray chambers using nozzles and water amounts which are not in accordance to practical field conditions.

Glyphosate, the most important generic active ingredient produced of the world is the most active patent area by far in order to improve glyphosate performance. Many companies sell glyphosate and the type and amount of surfactant in glyphosate formulations varies greatly. Green and Beestman focused on new formulation and adjuvant technologies available to maximize performance and minimize safety and environmental impact of herbicides (Green and Beestman 2007). Even though governments have not approved many new chemicals for use with agrochemicals during the past decade, there is a rich record of patent applications and product introductions. Formulation technology is the principal mechanism agrochemical companies use to renew products when the initial patents covering the active expire. The adjuvant and formulation industry has done an impressive job finding useful combinations and new utilities of currently approved chemicals.

Current data suggest that surfactant efficacy may be the result of charged surfactants ability to diffuse away from the cuticle into the subtending apoplastic space, where they act directly on the plasma membrane to increase glyphosate uptake. Cationic polyoxyethylene tertiary amine surfactants are more effective than nonionic surfactants at promoting glyphosate phytotoxicity (Wyrill and Burnside 1976; Riechers 1992). Surfactants promoting greatest glyphosate phytotoxicity are required at higher concentrations than necessary for maximum reduction of the spray solution surface tension, indicating that their mode of action is not limited to increasing the spreading characteristics of the spray droplet (Sherrick et al. 1986). This observation suggests that effective surfactants are also involved in increasing the permeability of the cuticle, plasma membrane, or both in increasing foliar uptake of glyphosate and promoting phytotoxicity. Richard and Slife determined that cellular absorption may offer greater resistance to foliar glyphosate uptake than cuticular penetration (Richard and Slife 1979). They suggested that the negative charges associated with the cell wall and the negative membrane potential of the plasma membrane repel the anionic glyphosate molecule. Sherrick et al. hypothesized that the surfactant MON 0818, is able to penetrate the cuticle and act at the plasma membrane (Sherrick et al. 1986). These authors reported that less than 20 % of $[^{14}C]$MON 0818 applied to field bindweed leaves was recovered in combined surface and chloroform washes, indicating surfactant penetration past the cuticle into underlying tissue.

Riechers et al. suggested that surfactant efficacy involves, at least partially, its ability to diffuse out of the cuticle into the apoplast where it alters membrane permeability to glyphosate (Riechers et al. 1994).

On the other hand, systematic studies conducted by and Nalewaja and co-workers indicate that surfactants of low ethylene oxide (EO) content may be optimal for promoting the uptake of lipophilic pesticides ($\log P > 3$), while those of high EO content were more beneficial for the uptake of hydrophilic compounds ($\log P < 0$) (Stock et al. 1993, 1992; Nalewaja et al. 1996). For compounds of intermediate lipophilicity, uptake is independent on the EO content of the added surfactant. The results were later confirmed by other studies on leaves and also on isolated cuticles (Nalewaja et al. 1996; Sharma et al. 1996; Coret and Chamel 1995).

One of the best way to evaluate the efficacy of glyphosate is measuring the efficiency of EPSPS (5-enolpyruvylshikimate 3-phosphate synthase) inhibition. Starting with a dose that is sprayed from a nozzle, only a fraction is foliarly retained, absorbed, translocated, and ultimately delivered to the plastids where EPSPS is localized. Each of these processes is in turn impacted by many physical, environmental, and physiological variables. For example, foliar retention can be affected by spray interception and droplet rebound which can be affected by plant morphology (e.g., leaf orientation and cuticle structure), environmental conditions (e.g., temperature and humidity), and surfactant concentration and droplet size (De Ruiter et al. 1990; Feng et al. 2003a; Buhler and Burnside 1987; Liu et al. 1996; Casely and Coupland 1985). Absorption is a major barrier for glyphosate efficacy and is affected by both surfactant class and concentration (De Ruiter et al. 1996; Denis and Delrot 1997). The efficacy of the tallow amine based cationic surfactants has been attributed to effective cuticle disruption (Feng et al. 1998; Ryerse 2001; Feng et al. 1999). Absorption is also impacted by the concentration gradient between the droplet and leaf, and efficacy enhancement has been reported at low spray volumes (Cranmer and Linscott 1990; Duncan Yerkes and Weller 1996; Feng et al. 2003a).

Glyphosate is translocated in the phloem from source to sink tissues following the sucrose gradient (McAllister and Haderlie 1985; Gougler and Geiger 1984). The excellent systemicity of glyphosate is derived from its unique combination of three acidic and one basic groups, and loss of any one of its functional groups resulted in decreased translocation (Bromilow and Chamberlain 2000). How glyphosate is loaded into the phloem is not well understood, but may involve phosphate transporters (Morin et al. 1997; Denis and Delrot 1993). Reductions in photoassimilate production and translocation ultimately reduce glyphosate translocation (Geiger et al. 1999). This self-limitation effect reduces the time window in which glyphosate can be efficiently translocated.

In the end, a plant that has been treated with glyphosate will die only if all the tissues have been killed. Any surviving tissue provides the opportunity for the plant to re-grow under favorable environmental conditions. The fate of individual tissues is decided based on whether a sufficient concentration of glyphosate was

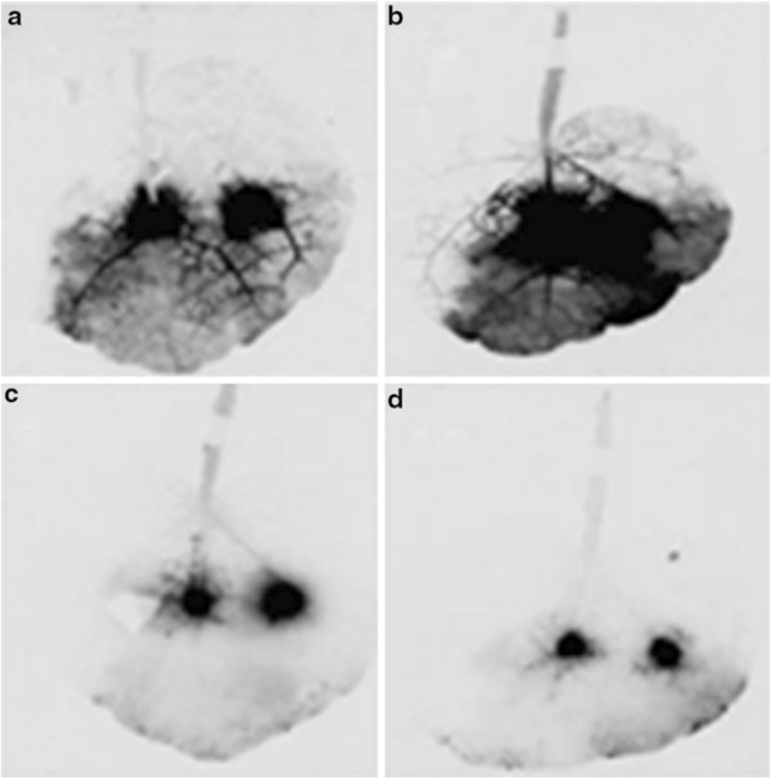


Fig. 7.8 Analysis by autoradiography of leaves with [^{14}C]glyphosate in MON0818 (0.1 %) as a function of harvest time: 2.5 (**a**), 5.0 (**b**), 24 (**c**) and 48 HAT (**d**) (Reprint from Feng et al. (2003b))

attained to inhibit EPSPS. Feng et al. examined the role of glyphosate distribution and tissue sensitivity in overall efficacy (Feng et al. 2003b). The process by which glyphosate is exported out of the treated leaf was examined by autoradiography. A sub-lethal dose of [^{14}C]glyphosate was formulated in 0.1 % MON0818 (tallow amine ethoxylated an nonylohenol ethoxylated mixture) and applied as two 1 μl droplets to the first leaf of 3.5 leaf velvetleaf plants. At various times (2.5, 5.0, 24, and 48 h after treatment, HAT) the treated leaf was excised and washed with water to remove surface residues (Fig. 7.8). Exposure of tissues to X-ray film allowed visualization of glyphosate that was in the leaf and provided a time course of glyphosate leaf export.

The studies used velvetleaf as a model and [^{14}C]glyphosate as the marker, and showed that plant response to glyphosate was impacted by both differential tissue distribution as well as sensitivity. The second conclusion is that the amount of

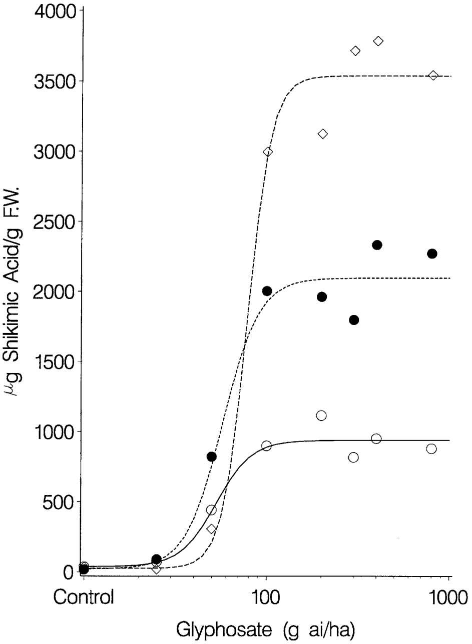


Fig. 7.9 Accumulation on shikimic acid in the third leaf of 3-week-old rape 48 h (◇), 24 h (•) and 6 h (○) after spraying with glyphosate (Reprint from Harring et al. (1998))

glyphosate delivered to tissues is linearly proportional to dose. This means that the dose does not change how glyphosate is distributed only how much is distributed. The current understanding is that whole plant efficacy is dependent on application of a dose of glyphosate that results in sufficient uptake and distribution to attain the lethal threshold in all tissues quickly and before the onset of self-limitation.

On the other hand, accumulation of shikimic acid was related to the dose of glyphosate by a nonlinear logistic dose response models as early as 5 h after spraying (Fig. 7.9). Within the same period shikimic acid accumulation made it possible to distinguish between a formulation of the pure isopropylamine salt of glyphosate and formulations containing different surfactants. ED50 (effective dose 50) estimates based on accumulation of shikimic acid gave a good indication of the relative strength of the evaluated glyphosate formulations. Ranking of ED50 based on accumulation of shikimic acid was the same as achieved by visual assessment of plant death 14 days after spraying.

Wan Kim and Amrhein found glyphosate induced accumulation of shikimic acid within 24 h after treatment of tomato (Wan and Amrhein 1995). Harring et al. studied the glyphosate action on phenylalanine ammonia-lyase activity and shikimic acid accumulation (Harring et al. 1998). Plants sense glyphosate toxicity within hours after application resulting in changes in carbon allocation and photosynthesis (Geiger and Bestman 1990).

7.12 Replacement of Fatty Amines and Nonylphenol Ethoxylated by New Renewable Resources-Based Surfactants

The selection of the type of formulation, active ingredient concentration, selection of the proper adjuvant and amount to maximize performance, maintaining product stability, all while insuring the toxicological properties of the product should meet customer, market and regulatory requirements. There is increasing regulatory and public pressure to decrease the amount of pesticides released into the environment. The challenge is to maintain and safeguard their efficiency with effective adjuvants. The use of petrochemical based surfactants like nonylphenol ethoxylates and fatty amine ethoxylates have declined significantly in the past decade, due to the ecological and toxicological reasons. Hence, there is continuing demand for alternatives based on a renewable source.

Run-off, leaching, adsorption and biodegradation are some of the possible exposure routes and main fate processes. Potential transport routes via rainwater may be either horizontal as run-off ending up in surface waters or vertical leaching to groundwater. Another fate route is adsorption to soil or biological material such as plants, plant roots and plant debris or micro-organisms in the soil. Additionally, the adjuvants may be biodegraded either aerobically or anaerobically.

The effects of nonylphenol ethoxylates and nonylphenol in the environment have been extremely controversial. Concerns first emerged in 1983–1984 when Giger and coworkers from Switzerland established that nonylphenol ethoxylates and products of degradation were more toxic to aquatic life than their precursors (Giger et al. 1984).

The first evidence that alkylphenols could be oestrogenic was published in 1938 by Dodds and Lawson but it was Soto and co-workers who accidentally observed that nonylphenol, which was employed in the manufacture of the test tubes used in their experiments, was capable of initiating proliferation in breast tumour cells as if oestrogens were present (Dodds and Lawson 1938; Soto et al. 1991). Endocrine disrupters can disturb the hormonal system by mimicking the occurrence of natural hormones, blocking their production or by inhibiting or stimulating the endocrine system. Nonylphenol was found to mimic the natural hormone 17β-oestradiol by competing for the binding site of the oestrogen receptor (Fig. 7.10a), due to their structural similarity (Fig. 7.10b) (Lee and Lee 1996; White et al. 1994).

For nonylphenol to exhibit endocrine activity the para-position of the phenolic OH-group and the branched aliphatic side chain appear to be determinant, meaning that not all nonylphenol isomers are capable of inducing oestrogenic activity (Kim et al. 2004; Odum et al. 1997; Tabira et al. 1999). 17β-oestradiol is a natural hormone that influences the development and maintenance of the female sex characteristics, and the maturation and function of accessory sex organs and it is also involved in the neuroendocrine and skeletal systems and is capable of promoting carcinogenicity in target tissues (Lee and Lee 1996; Alberts et al. 1983). Hence, nonylphenol is expected to initiate a variety of responses in organisms. Recently

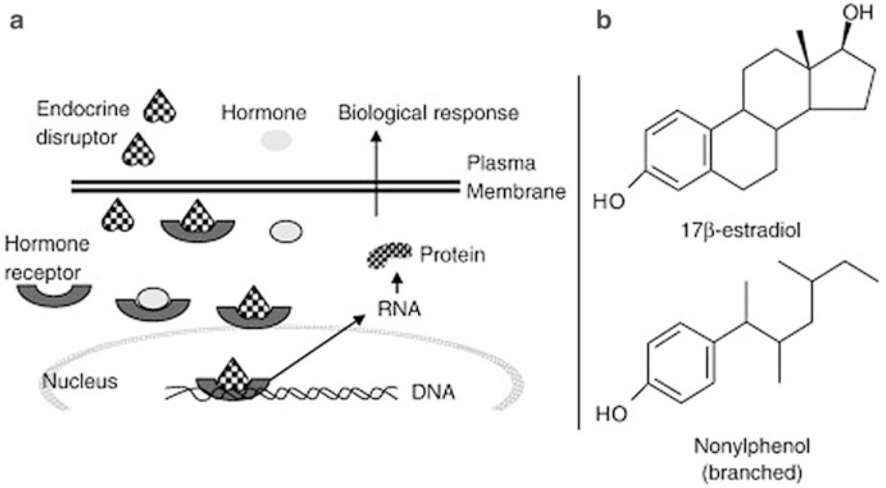


Fig. 7.10 Competition for the oestrogen binding receptor between nonylphenol and 17b-oestradiol in the cell (Reprint from Soares et al. (2005))

it has also been established that nonylphenol has antiandrogenic activity, i.e., is capable of interfering with the proper functioning of androgens that are essential for the normal development of males and their reproductive systems (Lee et al. 2003).

The responses of the endocrine system to nonylphenol have been thoroughly studied in different organisms (White et al. 1994; Laws et al. 2000). For instance, nonylphenol was capable of inducing the production of female proteins in rainbow trout (Oncorhynchus mykiss) at 20.3 mg/l, medaka fish (Oryzias latipes) exposed to 0.1 mg/l nonylphenol, and the platyfish (Xiphophorus maculates) testis morphology and male fertility were negatively affected at nonylphenol concentrations $\geq$0.96 mg/l after 4 weeks of exposure (Jobling et al. 1996; Tabata et al. 2001; Kinnberg et al. 2000).

According to the data above showed, nonylphenol ethoxylates compounds have therefore been added to Annex I to Regulation (EC) No 689/2008 of the European Parliament and of the Council concerning the export and import of dangerous chemicals (OJ L 204, 31.7.2008, p. 1–35). The pesticides agreed as ‘priorities for action’ are listed here (updated in 2004), as well as a list of substances of ‘possible concern’ including 98 pesticides (updated in September 2005).

However, many other countries, including China, India and several South American countries use and produce nonylphenolic compounds in large amounts and no action has been taken by any of these countries to reduce or eliminate their usage. Nonylphenol ethoxylates are being replaced by other surfactants in most European, Canadian and Japanese markets, mainly by alcohol ethoxylates (Krogh et al. 1997). These surfactants are less efficient but considered to be environmentally safer as they degrade more rapidly (Campbell 2002). However, few studies have been performed on the metabolites that are produced as a result of degradation of alcohol ethoxylates and it has been recently pointed out that their degradation gives rise to compounds with low water solubility and these adsorb to the sludge solids (Soares et al. 2005).

Meanwhile, tallow amine ethoxylates are the market reference of built-in adjuvants for glyphosate since many years, due to the excellent weed control performance they provide. However due to their toxicity profile there is a growing demand for alternatives with reduced labelling.

Traditionally, tallow amine ethoxylates (TAM-EO) were the built-in adjuvant of choice for standard isopropylamine (IPA) glyphosate 360 a.e./l formulations. These products are mediocre surfactants from a physico-chemical point of view, as indicated by fairly high surface tension and contact angle values. However, they are excellent adjuvants: it is believed that they act by facilitating the penetration of glyphosate, a relatively hydrophilic compound, through the rather hydrophobic cuticle which covers the external surface of higher plants, due to the disruption of cell walls allowing.

TAM-EOs and more especially TAM-15 EO and TAM-20 EO are harmful and hazardous for the environment. Quite unusual for a pesticide formulation is the co-formulant considered to be more toxic than the active ingredient. Glyphosate formulations with reduced labelling but with similar potency are therefore required in today's market.

The main disadvantages of these products is the high risk of damage to the eyes, the high toxicity to aquatic organisms, even in the concentration levels used in the formulation of glyphosate (8–15 %) and its high content of 1.4 dioxane (up to 25,000 ppm) due to the use of ethylene oxide during the process of manufacture of TAM-EO.

Several references were found in the literature about the toxicity of POEA (van Ginkel et al. 1993). TAM-EO has got more toxicity due to their high toxic by-products, without alkyl chain, resulting from the biodegradation process.

Finally in 2000, Bean and Cutler noted the low compatibility of alkoxylated alkylamine surfactants in general with high-strength glyphosate concentrates (Bean and Cutler 2000). This, in turn, has triggered the development of suitable formulants. Another driving force for new glyphosate additive developments is to save costs since the market has polarised into performance and low-cost brands since 2008. Many of the 700 glyphosate patent publications are directed at this issue, but still most of the improved adjuvant systems still contain amine-based surfactants. The current market situation could be called "the era of the small difference" where continually improved formulations are essential for success (Pimentel 1997).

7.13 Trends and Perspectives in Agrochemicals Formulations

The history of agricultural adjuvants dates back to eighteenth and nineteenth centuries when additives such as pitch, resins, flour, molasses, and sugar were used with lime, sulfur, copper, and arsenates to improve "sticking" and biological performance by modifying the physical and chemical characteristics of the applied mixture. Fundamentally, the goal of using adjuvants has stayed the same. Using substances that are inactive when used alone to improve the performance and application of an active ingredient by modifying the physical and chemical characteristics of the spray mixture is a fundamental part of all agrochemical research.

Despite the significance of agrochemicals use for pest control, the environmental problems caused by overuse of agrochemicals have brought scientists and publics much concern in recent years (Dayan et al. 2009). Of the reasons for this are (1) the high toxicity and non-biodegradable of agrochemicals; (2) the lack of scientific formulations. Thus, formulation scientists now are facing the challenge to explore novel green or environmental friendly agrochemical formulations to improve the biologic efficacy and develop techniques that can be employed to reduce pesticide use while maintaining plant protection. The tremendous increase in crop yields associated with the 'green' revolution has been possible in part by the discovery and utilization of chemicals for pest control. However, concerns over the potential impact of pesticides on human health and the environment has led to the introduction of new pesticide registration procedures, such as the Food Quality Protection Act in the United States. These new regulations have reduced the number of synthetic pesticides available in agriculture. Therefore, the current paradigm of relying almost exclusively on chemicals for pest control may need to be reconsidered. New pesticides, including natural product-based pesticides are being discovered and developed to replace the compounds lost due to the new registration requirements. Dayan et al. covered the historical use of natural products in agricultural practices, the impact of natural products on the development of new pesticides, and the future prospects for natural products-based pest management (Dayan et al. 2009).

7.14 New Methodologies in Agrochemicals Formulation

7.14.1 Microemulsions and Nanoemulsions

Microemulsions are considered as thermodynamically stable colloidal dispersions that are optically transparent or translucent with drop size in the range of 100–200 nm (Prince 1977). Thus, microemulsion may be regarded as one phase system (Lindman and Danielson 1981). As indicated above, the cloud point is one of the specific characteristics of the microemulsions. When the temperature of the microemulsion system is increased, the solubility of non-ionic surfactant decreases. The cloud point of microemulsion can be defined as the temperature at which the transparent microemulsion solution becomes cloudy, i.e. from one phase to two phases or three phases (Strey 1996).

It is common knowledge that by hydrating of polyethylene oxide group (PEO) chain, non-ionic surfactant is dissolved in water medium, but it may dissociate with water as a result of dehydration when the temperature exceeds its cloud point. The cloud point increases with increasing the amount of ethylene oxide groups in a chain, i.e. the higher hydrophilicity of non-ionic surfactant, the higher the cloud point. The cloud point is also affected by the concentration of the surfactant solution and the electrolytes in the aqueous solution. In the later case, usually lower the cloud point (Yoshihara et al. 1995; Saito and Shinoda 1967; Minanaperez et al. 1995; Tadros 1994). Chen et al. described, two new-types of pesticide microemulsions used for control *Liriomyza* spp., namely 16 wt % beta-cypermehtrin (inside microemulsion xylene oil droplets) plus monososultap (dissolved in water medium) and 20 % abamectin (inside microemulsion xylene oil droplets) plus monososultap (in the water medium) were prepared (Chen et al. 2000). The effects of agrochemical concentration, various surfactants at various concentrations on the cloud points of microemulsions have been studied. The stability of microemulsions containing 5 wt % abamectin and 1 wt % beta-cypermethrin is also discussed. Similar to the cloud point of surfactant aqueous solution, at constant surfactant concentration the cloud point of the agrochemical microemulsions increases as the hydrophilicity of the surfactant increases. The cloud point of the formulated microemulsions depends on the characteristics of the agrochemical, the kinds and the amounts of the added surfactant and co-surfactant.

The results above described shown that the values of the cloud point of microemulsions were depended on the nature of agrochemical, the surfactants used and the concentration of surfactants. Surfactants with higher HLB value at same concentration produce more stable agrochemical microemulsions, i.e. with higher cloud point. The results showed that the match between surfactant and oil phase or pesticide oil phase was the key to formulate stable microemulsions. However, the water quality was showed almost no effect on the cloud point of the agrochemical microemulsions in the studies.

Meanwhile microemulsions, which contain non-polar agrochemicals, usually have higher cloud points than those of containing polar ones, especially electrolytic agrochemicals. As discussed, higher cloud points can be obtained with an increase in surfactant concentration, but it is more reasonable to use more co-surfactant rather than surfactant, because the former is much cheaper.

On the other hand, Nanoemulsions have uniform and extremely small droplet sizes, typically in the range of 20–100 nm (Forgiarini et al. 2001). In addition, high kinetic stability, low viscosity and optical transparency make them very attractive systems for many industrial applications; for example, in agrochemicals for pesticide delivery (Lee and Tadros 1982). Wang et al. investigated potential applications of the system developed with water insoluble pesticide, β-cypermethrin (β-CP), incorporated into the precursor microemulsion concentrate (Wang et al. 2007). The effect of this active pesticide on stabilities of the concentrate, and the corresponding nanoemulsion, were also investigated. The incorporation of β-CP in the concentrate showed no effect on the phase behavior when present at less than 12 wt %. Compared with the commercial β-CP microemulsion, the excellent stability of sprayed solution diluted from the concentrate makes this system an ideal candidate as a water-insoluble pesticide delivery system. Thus, the application of the new methodology designing by spray formulations of β-CP may enable a reduction in the applied amounts, relative to those formulated as O/W microemulsions. These characteristics make the new methodology promising from both environmental and economical points of view.

7.14.2 Liposomes

Liposomes are structures made of lipid bilayers forming one or more concentric spheres which entrap part of the solvent in which they freely float, into their interior. Their unique properties have triggered numerous applications in various fields of science and technology, from basic studies of membrane function to the use as carriers of very different substances. In agriculture, they can be used to improve the efficacy of different biocides and to deliver some essential nutrients (Lasic 1993). Herbicides, fungicides and pesticides are rapidly washed from the leaves of plants and encapsulation in liposomes may prolong the action of these agents on plants and reduce the damage in soil cultures. Pons and Estelrich described the optimization of a cheap and easy method of preparing liposomes (Pons and Estelrich 1996). Among the studied formulations there are some with a high stability and this property makes them very suitable to be used as an agrochemical product.

7.14.3 Nanomaterials

Materials with a particle size less than 100 nm in at least one dimension are generally classified as nanomaterials. The development of nanotechnology in conjunction with biotechnology has significantly expanded the application domain of nanomaterials in various fields. However in the field of agriculture, the use of nanomaterials is relatively new and needs further exploration.

Khot et al. summarized the developments and application of novel nanomaterials in agriculture, and described nanopesticides and its applications. Nanopesticides “involve either very small particles of pesticidal active ingredients or other small engineered structures with useful pesticidal properties” and can increase the dispersion and wettability of agricultural formulations (i.e., reduction in organic solvent runoff), and unwanted pesticide movement. Nanomaterials and biocomposites exhibit useful properties such as stiffness, permeability, crystallinity, thermal stability, solubility, and biodegradability needed for formulating nanopesticides. Nanopesticides also offer large specific surface area and hence increased affinity to the target. Nanoemulsions, nanoencapsulates, nanocontainers, and nanocages are some of the nanopesticide delivery techniques that have been discussed recently for plant protection (Khot et al. 2012).

7.15 New Surfactants and Additives Apply to Agrochemicals Formulation

There is increasing regulatory and public pressure to decrease the amount of pesticides released into the environment. The current trends in the development of pesticide formulations are increased enormously to meet the needs of environmental safety, eliminate organic solvents or to improve the activity and persistence of the active ingredient (Knowles 2008).

7.15.1 Alkyl Polyglycosides

Alkyl polyglycosides or APG's are non ionic surfactants with a hydrophilic saccharide instead of an ethylene oxide chain. The alkyl chain has 8–16 carbons. APGs are water soluble with excellent adjuvant properties. APGs are made from renewable raw materials and can be put into very concentrated liquid of dry formulations (Pompeo et al. 2005). They are called "green surfactants" because they are very safe to the environment.

Short chain APGs show decent properties as wetting and penetrating agents and offer a high tolerance to saline solutions though they are non-ionic, and do not exhibit a cloud point typical for alkoxylates (Nickel et al. 1996). The importance of nonionic APGs for glyphosate was first recognized by Syngenta as potentiators for glyphosate (Burval and Chan 1995).

Alkyl polyglycosides (APG) are superior surfactants with outstanding wetting properties and are used as adjuvants for pesticides as they improve the spreading and enhance the uptake of the pesticides (Garst 1997). Nonetheless, the effect of APGs on weed control of glyphosate cannot match industry standards. Advantageously however, as compared to TAM-EO, APGs are generally classified as non-toxic and ready biodegradable. Several options were explored to take advantage of the benefits of APGs as high performance wetting agents whilst optimising the weed control.

A new class of non-ionic surfactants resulting from the direct ethoxylation of alkyl and/or alkenyl polyglycosides was designed as possible alternatives to TAM-EO (Behler and Clasen 2006). Their performance as adjuvants for glyphosate was assessed in greenhouse trials on two model plant species. The new derivatives were compared to TAM-EO and to straight APG. According to the greenhouse data, alkoxylated alkyl polyglycosides showed good weed control almost reaching performance of TAM-EOs and surpassing efficiency of standard APG. Alkoxylated alkyl polyglycosides exhibit also a much better toxicological profile compared to TAM-EOs reducing the risk to end-users.

7.15.2 *Ethoxylated Saccharose Esters*

In 2007, ethoxylated APGs were introduced. Due to their hydrophilic properties, they turned out to be suitable glyphosate potentiators and adjuvants (Abribat et al. 2007). However, their low lipophilicity makes them not compatible in oil based formulations such as emulsifiable concentrate (EC) or concentrated oil-in-water emulsion (EW) and consequently, new lipophilic surfactants based on ethoxylated saccharose esters have been developed.

In a recent application, Mainx and Hofer described alkylene oxide adducts of oligosaccharides like saccharose (Mainx and Hofer 2009). Their esterification leads to a new chemical class of label-free nonionic surfactants. Selected representatives of this class of chemicals showed outstanding results in boosting the performance of crop protection products in greenhouse studies. Indeed, the protective property of azoxystrobin applied with these new ethoxylated saccharose esters was more effective than the industry standards, such as nonylphenol ethoxylated and isotridecyl alcohol 6 EO. In curative tests, the activity of the fungicide epoxiconazole was improved as well, although the effects were less pronounced.

Epoxiconazole was improved as well, although the effects were less pronounced and even the activity of glyphosate was enhanced. Ethoxylated saccharose esters show a good toxicological and ecotoxicological profile. Their behaviour in pesticide formulations and tank mix solutions is excellent, so in total, they can be considered as a novel suitable class of adjuvants and surfactants for pesticide formulations.

The studies above mentioned showed that ethoxylated saccharose esters have an excellent potential as new adjuvants and emulsifiers in agrochemical compositions. Especially with fungicides at low concentrations, they show extraordinary results in improving the activity of the active ingredients suggesting their suitability as both, tank mix adjuvants and inerts for incan formulations. Due to good compatibility with most new solvents, this new chemical class of surfactants can also be considered to become suitable components in all pesticide formulations either alone or in combination with other nonionic or anionic surfactants.

7.15.3 *Dimethylethanolamine Based Esterquats*

Esterquat chemistries are widely used in the commercial laundry market as fabric softeners. They have been used since the 1970s as biodegradable alternatives to dihydrogenated tallow dimethyl ammonium chloride (DHTDMAC) chemistries. However, the use of esterquats in agrochemical formulations has not been thoroughly explored and would represent a biodegradable alternative chemistry (Zoller 2009). In addition, esterquats may offer reduced eye irritation or improved ecotoxicity profiles to an industry that is becoming ever more scrutinized for such formulation improvements.

Malec et al. explored the use of esterquats based on dimethylethanolamine (DMEA) in agricultural formulations (Malec et al. 2009). It was determined that DMEA based esterquats can function as wetters or spreaders, but can also act as emulsifiers. The surface active properties and aquatic toxicity of esterquats as surfactants will be explored as well. The esterquats have lower critical micelle concentrations, lower equilibrium surface tensions, and faster wetting times than traditional agricultural surfactants.

Various formulations were explored including herbicides, insecticides, and fungicides. These formulations included delivery systems such as soluble concentrates (SL) and emulsifiable concentrates (EC). The formulations were evaluated and in many cases provided performance properties that were equal to current standards for commercial products. Greenhouse trials were conducted evaluating the effectiveness of esterquats in glyphosate (*N*-(phosphonomethyl) glycine) formulations. It was found that esterquats were successful glyphosate adjuvants, utilizing lower surfactant use rates while offering equal efficacy to commercial products. Additionally, glyphosate formulations using DMEA esterquats have lower eye irritation compared to other commercial standard glyphosate surfactants. The aquatic toxicity of DMEA esterquats was also studied and the DMEA esterquats were found to be less toxic than TAM-EO.

The studies showed that DMEA esterquats may serve a valuable function in agrochemical formulations. They offer improved biodegradability, lower eye toxicity, improved wetting, spreading, and penetration, and comparable aquatic toxicity to commercial surfactants already in use in agrochemicals.

7.15.4 Chitosan Derivatives

Chitosan based polymeric micelle due to its outstanding biologic properties and functions such as biodegradability, biocompatibility, insecticidal and antibacterial activity, has been widely researched or applied in the fields of agriculture, medicine, pharmaceuticals, functional food in the last decade (Chellat et al. 2000; Risbud and Bhonda 2000; Badawy et al. 2004; Hejazi and Amiji 2003; Kumar et al. 2004; Rabea et al. 2005). However, chitosan has no amphiphilicity, cannot form micelle and load drug directly. In recent years, chitosan-based micelle system has been developed by introducing hydrophobic and/or hydrophilic groups to the chitosan backbone (Zhang et al. 2008). Amphiphilic chitosan derivatives which grafted sulfuryl as hydrophilic moieties and octyl as hydrophobic moieties had been reported (Zhang et al. 2003, 2008).

Lao et al. described novel amphiphilic chitosan derivatives designed and synthesized by grafting octadecanol-1-glycidyl ether to amino groups, sulfate to hydroxyl groups (e.g. N-(octadecanol-1-glycidyl ether)-O-sulfate chitosan (NOSCS)) (Lao et al. 2010). Rotenone as a model drug was chosen and used to assess the potential loading capability of novel chitosan derivatives. The insecticide rotenone was loaded and formed about 116.4–216.0 nm nanoparticles, and its solubility in

NOSCS micelles aqueous solution was increased largely. The highest concentration of rotenone was up to 26.0 mg/mL (NOSCS- 1), which was about 13,000 times that of free rotenone in water (about 0.002 mg/mL).

7.15.5 Ammonium Sulphate and Sulphated Glycerine as Additive

The leaf cuticle and plasma membrane have been identified as barriers limiting glyphosate activity (Riechers et al. 1994; Denis and Delrot 1993). Neither glyphosate nor its different salts are effective in overcoming these barriers easily without appropriate surfactants (Buhler and Burnside 1983b; Jordan 1981). Cationic surfactants have been found to be more effective than nonionic surfactants in increasing efficacy (Wyrill and Burnside 1976; Riechers et al. 1995). The addition of ammonium sulphate (AMS), an inorganic salt, to the glyphosate spray solution improved the efficacy of the herbicide (Blair 1975). Additionally, it has been found that salts dissolved in water used as the carrier for glyphosate may reduce its effectiveness, particularly calcium and magnesium salts. These salts have a positive charge and may associate with the negatively charged glyphosate molecule, replacing the isopropylamine or diammonium salts found in the formulated glyphosate product. AMS reduces the formation of calcium–glyphosate complexes on these leaves and therefore improves performance (Hartzler 2001). The inverse relationships between weed growth parameters and increasing concentration levels of AMS suggest that the ability of AMS to enhance glyphosate activity is to a large extent concentration dependent (Aladesanwa and Oladimeji 2005).

Glycerine and ammonium sulphate have both been popular additives in the long-held practice of adding chemical agents (adjuvants) to improve biological efficacy in crop protection sprays (Gednalske and Herzfeld 1994). Glycerine, a polyol of natural origins (triglycerides), is one of the principle building blocks of plant tissues. This biocompatibility as well as glycerine’s humectancy is strong contributors to its adjuvancy with additional benefit as a hydrotrope to homogenize water-based spray solutions (Heldt et al. 2000). Ammonium sulphate is a proven sequestrant of hard water cations as well as a nitrogen source benefiting herbicides of diverse modes of action (Buhler and Burnside 1983a). One difficulty with ammonium sulphate solutions are their ionic strength and the difficulty that presents in creating shelf-stable blends with surfactants (Gednalske and Herzfeld 1994).

Anderson presented the reaction product(s) resulting from sulphating glycerine show strong adjuvant activity with herbicides (Anderson 2010). As with ammonium sulphate, the adjuvant activity of sulphated glycerine includes both, sequestering cations commonly found in hard water as well as increased nitrogen for non-complexing herbicides. The field treatments including sulphated glycerine, demonstrated statistically superior weed control when compared to un-sequestered reference samples. These “hard water” treatments including sulphated glycerine were statistically equivalent to control observed for glyphosate sprays prepared with de-ionized water. The increased efficacy of the herbicide glufosinate was demonstrated when using ammonium sulphate or sulphated glycerine as an adjuvant. Both of these biological observations were confirmed with rates of sulphated glycerine significantly lower than current label rates for ammonium sulphate.

7.16 Conclusion

Uptake of pesticides into plant foliage varies with plants and chemicals, and can be greatly influenced by adjuvants and environmental conditions. Adjuvants usually have multiple functions in relation to pesticide efficacy. Increasing the foliar uptake of active ingredients is of particular importance for herbicides, growth regulators, and defoliants. It is known that the penetration of pesticides into plant leaves is related to the physicochemical properties of the active ingredients, especially molecular size and lipophilicity. However, the uptake rate of a compound cannot be predicted by either of them or even combination of them. For a specific chemical, uptake varies greatly with plant species and there is no simple method at the moment to quickly evaluate the leaf surface permeability of a plant.

Environmental conditions have an important influence on herbicide efficacy. In particular, the effect of humidity on herbicide uptake has been attributed to changes in cuticle hydration and droplet drying. Herbicide uptaking slows or stops when herbicide droplets dry, it was suggested that humectants or wetting agents could enhance herbicide uptake by keeping droplets moist, maintaining the herbicide in solution, and keeping it available for uptake.

Various adjuvants are being used to increase the penetration of pesticides into target plant foliage, but their effects vary with chemicals and plant species. The mechanisms of action of adjuvants in enhancing pesticide uptake remain unclear despite the effort made during the last three decades. Modern analytical and microscopic techniques provide powerful tools to deepen our understanding in this issue. However, a more multidisciplinary approach is urgently needed to elucidate the transcuticular diffusion behaviour of pesticides and the mode of action of adjuvants. A better understanding of the foliar uptake process should lead to a more rational use of pesticides and minimize their negative impact on the environment. Therefore, a systematic study on the complex interaction between active ingredients, surfactants and plants should lead to a more rational and cost-effective use of surfactants in weed control.

On the other hand, commercial glyphosate formulations are more acutely toxic than glyphosate, since the amount of Roundup® required to kill rats is about 1/3 of the amount of glyphosate alone. Similar results have been obtained in cell division, thus indicating a synergy between glyphosate and Roundup® formulation products. Although glyphosate is already one of the most used xenobiotics in modern agriculture, we should expect an increasing utilization of glyphosate largely due to the number of transgenic plants developed to be tolerant to this herbicide. Fatty amine ethoxylates or co-formulant called "inert ingredients" used in Roundup® are greatly responsible for the observed toxicity at the bioenergetic level. Quite unusual for a pesticide formulation is the co-formulant considered to be more toxic than the active ingredient. Glyphosate formulations with reduced labelling but with similar potency are therefore required in today's market.

The fact that the adjuvant could be more toxic than the active ingredient in one of the most active ingredient used pesticides together with the need that more effectiveness is required to reduce the environmental effect of xenobiotics has lead to the development of new adjuvants, e.g. more than 600 patent of glyphosate formulations have been published in the last 12 years.

It is important to point out that there is increasing regulatory and public pressure to decrease the amount of pesticides released into the environment. The challenge is to maintain and safeguard their efficiency with effective adjuvants. The use of petrochemical based surfactants like nonylphenol ethoxylates and fatty amine ethoxylates have declined significantly in the past decade, due to the ecological and toxicological reasons. Hence, there is continuing demand for alternatives based on a renewable source. Suppliers are developing new surfactants and new surfactants formulations based on natural products such as vegetable oils, lecithin, sugars, amino acid and others. Microemulsions, liposomes and nanoemulsions as emerging technologies in agrochemicals formulations have reduced the use of petrochemical solvents, e.g. xylene and improve the efficiency of biocides. The development of nanotechnology in conjunction with biotechnology has significantly expanded the application domain of nanomaterials in various fields. However in the field of agriculture, the use of nanomaterials is relatively new and needs further exploration.

These products will become more popular in the near future as a means of increasing product safety and enabling quicker product regulation.

References

Abribat B, Anderson T, Oester D (2007) Alkoxylated polyglycosides, next generation glyphosate potentiators. In: Gaskin RE (ed) Proceedings of the 8th international symposium on adjuvants for agrochemicals, ISAA, Christchurch

Aladesanwa RD, Oladimeji MO (2005) Optimizing herbicidal efficacy of glyphosate isopropylamine salt through ammonium sulphate as surfactant in oil palm (*Elaeis guineensis*) plantation in a rainforest area of Nigeria. Crop Prot 24:1068–1073

Alberts E, Kalverboer AF, Hopkins B (1983) Mother infant dialog in the first days of life an observational study during breast-feeding. J Child Psychol Psychiatry 24:145–161

Anderson TH (2010) Sulphated glycerine, a new sequestrant and adjuvant for herbicide sprays. In: Baur P, Bonnet M (eds) Proceedings of the 9th international symposium on adjuvants for agrochemicals, Dynevo, Leverkusen, pp 301–306

Annual Book of ASTM Standards (2006) Volume 11.04, E 1519-06a, ASTM International, West Conshohocken. www.astm.org

Badawy MEI, Rabea EI, Rogge TM, Stevens CV, Smagghe G, Steurbaut W, Höfte M (2004) Synthesis and fungicidal activity of new N, O-acyl chitosan derivatives. Biomacromolecules 5:589–595

Baker EA, Hayes AL, Butler RC (1992) Physicochemical properties of agrochemicals: their effects on foliar penetration. Pestic Sci 34:167–182

Banduhn MC, Frazier HW (1978) G 3780A surfactant: biodegradation in nature waters. report no. MSL-0488. Monsanto Company, St. Louis

Bauer H, Schönherr J (1992) Determination of mobilities of organic compounds in plant cuticles and correlation with molar volumes. Pestic Sci 35:1–11

Bean M, Cutler J (2000) Agrochemical composition. EP Patent 1006792

Becker M, Kerstiens G, Schönherr J (1986) Water permeability of plant cuticles: permeance, diffusion and partition coefficients. Trees 1:54–60

Behler A, Clasen F (2006) Method for the alkoxylation of alkyl/alkylene polyglycosides. EP Patent 1716163

Beyers SW (1995) Acute toxicity of Rodeo® herbicide to Rio Grande silvery minnow as estimated by surrogate species: plains minnow and fathead minnow. Arch Environ Contam Toxicol 29:24–26

Blair AM (1975) The addition of ammonium salt or phosphate ester to herbicides to control *Agropyron repens* (L) Beaux. Weed Res 15:101–105

Bromilow RH, Chamberlain K (2000) The herbicide glyphosate and related molecules: physicochemical and structural factors determining their mobility in phloem. Pest Manag Sci 56:368–373

Bromilow RH, Chamberlain K, Evans A (1990) Physicochemical aspects of phloem translocation of herbicides. Weed Sci 38:305–314

Buchholz A, Peter B, Schönherr J (1998) Differences among plant species in cuticular permeabilities and solute mobilities are not caused by differential size selectivities. Planta 206: 322–328

Buhler DD, Burnside OC (1983a) Effect of water quality, carrier volume, and acid on glyphosate phytotoxicity. Weed Sci 31:163–169

Buhler DD, Burnside OC (1983b) Effect of spray components on glyphosate toxicity to annual grasses. Weed Sci 35:124–130

Buhler DD, Burnside OC (1987) Effects of application variables on glyphosate phytotoxicity. Weed Technol 1:14–17

Burghardt M, Schreiber L, Riederer M (1998) Enhancement of the diffusion of active ingredients in barley leaf cuticular wax by monodisperse alcohol ethoxylates. J Agric Food Chem 46:1593–1602

Burval J, Chan JH (1995) Liquid phytoactive compositions. US Patent 5 468 718

Campbell P (2002) Alternatives to nonylphenol ethoxylates, Review of toxicity, biodegradation & technical-economic aspects. In: ToxEcology environmental consulting, Report for Environment Canada, Vancouver

Cano ML, Dorn PB (1996) Sorption of two model alcohol ethoxylate surfactants to sediments. Chemosphere 33:981–994

Casely JC, Coupland D (1985) Environmental and plant factors affecting glyphosate uptake, movement and activity. In: Grossbard E, Atkinson D (eds) The herbicide glyphosate. Butterworth and Co, London, pp 92–123

Chefetz B (2003) Sorption of phenanthrene and atrazine by plant cuticular fractions. Environ Toxicol Chem 22:2492–2498

Chellat F, Tabrizian M, Dumitriu S, Chornet E, Rivard CH, Yahia LH (2000) Study of biodegradation behavior of chitosan-xanthan microspheres in simulated physiological media. J Biomed Mater Res 53:592–599

Chen B, Li Y (2007) Sorption of 1-naphthol by plant cuticular fractions. J Environ Sci 19:1214–1220

Chen F, Wang Y, Zheng F, Wu Y, Liang W (2000) Studies on cloud point of agrochemical microemulsions. Colloids Surf A 175:257–262

Chen B, Li Y, Guo Y, Zhu L, Schnoor JL (2008) Role of the extractable lipids and polymeric lipids in sorption of organic contaminants onto plant cuticles. Environ Sci Technol 42:1517–1523

Contardo-Jara V, Klingelmann E, Wiegand C (2009) Bioaccumulation of glyphosate and its formulation Roundup® Ultra in *Lumbriculus variegatus* and its effects on biotransformation and antioxidant enzymes. Environ Pollut 157:57–63

Cordiner JL (2004) Challenges for the PSE community in formulations. Comput Chem Eng 29:83–92

Coret J, Chamel A (1995) Effects and possible mode of action of some nonionic surfactants on the diffusion of glyphosate and chlorotoluron across isolated plant cuticles. Pestic Sci 43:163–166

Coupland D (1988) Factors affecting the phloem translocation of foliage applied herbicides. In: Aitken RK, Clifford DR (eds) British plant growth regulation 18. British Plant Growth Regulation Group Monograph, pp 85–112

Crafts AS (1960) Evidence for hydrolysis of esters of 2,4-D during absorption by plants. Weeds 8:19–25

Cranmer JR, Linscott DL (1990) Droplet makeup and the effect on phytotoxicity of glyphosate in velvetleaf (*Abutilon theophrasti*). Weed Sci 38:406–410

Dayan FE, Cantrell CL, Duke SO (2009) Natural products in crop protection. Bioorg Med Chem 17:4022–4034

De Ruiter H, Uffing AJM, Meinen E, Prins A (1990) Influence of surfactants and plant species on leaf retention of spray solutions. Weed Sci 38:567–572

De Ruiter H, Straatman K, Meinen E (1993) The influence of a fatty amine surfactant on foliar absorption and translocation of the trolamine salt and *iso*-octyl ester of 2,4-D. Pestic Sci 38:145–154

De Ruiter H, Uffing AJM, Meinen E (1996) Influence of surfactants and ammonium sulfate on glyphosate phytotoxicity to quackgrass (*Elytigia repens*). Weed Technol 10:803–808

Denis MH, Delrot S (1993) Carrier-mediated uptake of glyphosate in broad bean (*Vicia faba*) via a phosphate transporter. Physiol Plantar 87:569–575

Denis MH, Delrot S (1997) Effects of salt and surfactants on foliar uptake and long distance transport of glyphosate. Plant Physiol Biochem 35:291–301

Devine MD, Hall LM (1990) Implications of sucrose transport mechanisms for the translocation of herbicides. Weed Sci 38:299–304

Dodds EC, Lawson W (1938) Molecular structure in relation to estrogenic activity: compounds without a phenanthrene nucleus. Proc R Soc Lond B Biol Sci 125:222–232

Duncan Yerkes CN, Weller SC (1996) Diluent volume influences susceptibility of field bindweed (*Convolvulus arvensis*) biotypes to glyphosate. Weed Technol 10:565–569

Edser C (2007) Multifaceted role for surfactants in agrochemicals. Focus Surfact 3:1–2

Feng PCC, Ryerse JS, Sammons RD (1998) Correlation of leaf damage with uptake and translocation of glyphosate in velvetleaf (*Abutilon theophrasti*). Weed Technol 12:300–307

Feng PCC, Ryerse JS, Jones CR, Sammons RD (1999) Analysis of surfactant leaf damage using microscopy and its relation to glyphosate or deuterium oxide uptake in velvetleaf (*Abutilon theophrasti*). Pest Sci 55:385–386

Feng PCC, Chiu T, Sammons RD, Ryerse JS (2003a) Droplet size affects glyphosate retention, absorption and translocation in corn. Weed Sci 51:443–448

Feng PCC, Chiu T, Sammons RD (2003b) Glyphosate efficacy is contributed by its tissue concentration and sensitivity in velvetleaf (*Abutilon theophrasti*). Pest Biochem Physiol 77:83–91

Fernández Cirelli A, Ojeda C, Castro MJL, Salgot M (2008) Surfactants in sludge- amended agricultural soils. A review. Environ Chem Lett 6:135–148

Folmar LC, Sanders OH, Julin AM (1979) Toxicity of the herbicide glyphosate and several of its formulations to fish and aquatic invertebrates. Arch Environ Contam Toxicol 8:269–278

Forgiarini A, Esquena J, Gonzalez C, Solans C (2001) Formation of nano-emulsions by low-energy emulsification methods at constant temperature. Langmuir 17:2076–2083

Forster WA, Zabkiewicz JA, Riederer M (2004) Mechanisms of cuticular uptake of xenobiotics into living plants: 1. Influence of xenobiotic dose on the uptake of three model compounds, applied in the absence and presence of surfactants into *Chenopodium album*, *Hedera helix* and *Stephanotis floribunda* leaves. Pest Manage Sci 60:1105–1113

Foy CL (1987) Adjuvants: terminology, classification, and mode of action. In: Chow PNP, Grant CA, Hinshalwood AM, Simundson E (eds) Adjuvants and agrochemicals. CRC Press, Boca Raton, pp 1–15

Foy CL (1989) Adjuvants for agrochemicals: introduction, historical overview and future outlook. In: Chow PNP, Grant CA, Hinshalwood AM, Simundsson E (eds) Adjuvants and agrochemicals: II recent development, application, and bibliography of agro adjuvants. CRC Press, Boca Raton, pp 2–9

Franz JE, Mao MK, Sikorski JA (1997) Glyphosate: a unique global herbicide. In: ACS monograph, vol. 189, American Chemical Society, Washington, DC, pp 163–175

Gardner SC, Grue CE (1996) Effects of rodeo® and garlon 3A on nontarget wetland species in central Washington. Environ Toxicol Chem 15:441–451

Garst R (1997) New solutions for agricultural applications. In: Hill K, Rybinski W, Stoll G (eds) Alkyl polyglycosides. VCH, Weinheim, pp 131–137

Gednalske JV, Herzfeld RW (1994) Homogenous herbicidal adjuvant blend comprising glyphosate ammonium sulfate and alkyl polysaccharide. US Patent 5 356 861

Geiger DR, Bestman HD (1990) Self-limitation of herbicide mobility by phytotoxic action. Weed Sci 38:324–329

Geiger DR, Shieh WJ, Fuchs MA (1999) Causes of selflimited translocation of glyphosate in *Beta vulgaris* plants. Pest Biochem Physiol 64:124–133

Giesy JP, Dobson S, Solomon KR (2000) Ecotoxicological risk assessment for Roundup® herbicide. Rev Environ Contam Toxicol 167:35–120

Giger W, Brunner PH, Schaffner C (1984) 4-Nonylphenol in sewage-sludge: accumulation of toxic metabolites from nonionic surfactants. Science 225:623–625

Goldsborough LG, Brown DJ (1993) Dissipation of glyphosate and aminomethylphosphonic acid in water and sediments of boreal forest ponds. Environ Toxicol Chem 12:1139–1147

Gougler JA, Geiger DR (1984) Carbon partitioning and herbicide translocation in glyphosate treated sugar beet (*Beta vulgaris*). Weed Sci 32:546–551

Green JM, Beestman GB (2007) Recently patented and commercialized formulation and adjuvant technology. Crop Prot 26:320–327

Harring T, Streibig JC, Husted S (1998) Accumulation of shikimic acid: a technique for screening glyphosate efficacy. J Agric Food Chem 46:4406–4412

Hartley GS, Brunskill RT (1958) Reflection of water droplets from surfaces. In: Danielli JF, Parkhurst KGA, Riddiford AC (eds) Surface phenomena in chemistry and biology. Pergamon Press, New York, pp 214–223

Hartzler B (2001) Glyphosate- a review. Iowa State University, Ames, Iowa

Heinemann A (2010) Megatrends in agriculture. In: Proceedings of the 8th international symposium on adjuvants for agrochemicals. ISAA Society, Freising, pp 19–20

Hejazi R, Amiji M (2003) Chitosan-based gastrointestinal delivery systems. J Control Release 89:151–165

Heldt N, Zhao J, Friberg S, Zhang Z, Slack G, Li Y (2000) Controlling the size of vesicles prepared from egg lecithin using a hydrotrope. Tetrahedron 56:6985–6990

Henry CJ, Higgins KF, Buhl KJ (1994) Acute toxicity and hazard assessment of Rodeo, X-77 Spreader, and Chem-Trol to aquatic invertebrates. Arch Environ Contam Toxicol 27: 392–399

Hess FD, Foy CL (2000) Interaction of surfactants with plant cuticles. Weed Technol 14:807–813

Hochberg EG (1996) The market for agricultural pesticide inert ingredients and adjuvants. In: Foy CL, Pritchard DW (eds) Pesticide formulation and adjuvant technology. CRC Press, Boca Raton, pp 203–208

Holden WTC (1992) Future formulation trends – the likely impact of regulatory and legislative pressures. In: Brighton crop protection conference, vol. 11, BCPC, Brighton, pp 313–320

Holloway PJ (1993) Structure and chemistry of plant cuticles. Pestic Sci 37:203–232

Jeffree C (1996) Cuticles: an integrated functional approach. In: Kerstiens G (ed) Plant. BIOS scientific, Oxford

Jobling S, Sheahan D, Osborne JA, Matthiessen P, Sumpter JP (1996) Inhibition of testicular growth in rainbow trout (*Oncorhynchus mykiss*) exposed to estrogenic alkylphenolic chemicals. Environ Toxicol Chem 15:194–202

Jordan TN (1981) Effects of diluent volumes and surfactant on the phytotoxicity of glyphosate to bermuda grass (*Cynodon dactylon*). Weed Sci 29:79–83

Khot LR, Sankaran S, Maja JM, Ehsani R, Schuster EW (2012) Applications of nanomaterials in agricultural production and crop protection: a review. Crop Prot 35:64–70

Kim Y-S, Katase T, Sekine S, Inoue T, Makino M, Uchiyama T, Fujimoto Y, Yamashita N (2004) Variation in estrogenic activity among fractions of a commercial nonylphenol by high performance liquid chromatography. Chemosphere 54:1127–1134

Kindall HW, Pimentel D (1994) Constraints on the expansion of the global food supply. Ambio 23:198–205

Kinnberg K, Korsgaard B, Bjerregaard P, Jespersen A (2000) Effects of nonylphenol and 17 beta-estradiol on vitellogenin synthesis and testis morphology in male platyfish Xiphophorus maculatus. J Exp Biol 203:171–181

Kirkwood RC (1999) Recent developments in our understanding of the plant cuticle as a barrier to the foliar uptake of pesticides. Pestic Sci 55:69–77

Knowles A (2008) Recent developments of safer formulations of agrochemicals. Environmentalist 28:35–44

Krogh PH, Holmstrup M, Petersen SO, Jensen J (1997) Ecotoxicological assessment of sewage sludge in agricultural soil. In: Danish ministry for the environment, The Environmental Protection Agency, working report No. 69

Krogh KA, Halling-Sørensen B, Mogensen BB, Vejrup KV (2003) Environmental properties and effects of nonionic surfactant adjuvants in pesticides: a review. Chemosphere 50:871–901

Kumar MNVR, Muzzarelli RA, Muzzarelli C, Sashiwa H, Domb AJ (2004) Chitosan chemistry and pharmaceutical perspectives. Chem Rev 104:6017–6084

Lao SB, Zhang ZX, Xu HH, Jiang GB (2010) Novel amphiphilic chitosan derivatives: synthesis, characterization and micellar solubilization of rotenone. Carbohyd Polym 82:1136–1142

Lasic DD (1993) Liposomes from physics to applications. Elsevier, Amsterdam, pp 507–516

Laws SC, Carey SA, Ferrell JM, Bodman GJ, Cooper RL (2000) Estrogenic activity of octylphenol, nonylphenol, bisphenol A and methoxychlor in rats. Toxicol Sci 54:154–167

Lee PC, Lee W (1996) In vivo estrogenic action of nonylphenol in immature female rats. Bull Environ Contam Toxicol 57:341–348

Lee GWJ, Tadros TF (1982) Formation and stability of emulsions produced by dilution of emulsifiable concentrates. Part I. An investigation of the dispersion on dilution of emulsifiable concentrates containing cationic and non-ionic surfactants. Colloids Surf 5:105–115

Lee JF, Liao PM, Kuo CC, Yang HT, Chiou CT (2000) Influence of a nonionic surfactant (Trion X-100) on contaminant distribution between water and several soil solids. J Colloid Interface Sci 229:445–452

Lee HJ, Chattopadhyay S, Gong EY, Ahn RS, Lee K (2003) Antiandrogenic effects of bisphenol a and nonylphenol on the function of androgen receptor. Toxicol Sci 75:40–46

Lee JF, Hsu MH, Chao HP, Huang HC, Wang SP (2004) The effect of surfactants on the distribution of organic compounds in the soil solid/water system. J Hazard Mater 114:123–130

Li Y, Chen B (2009) Phenanthrene sorption by fruit cuticles and potato periderm with different compositional characteristics. J Agric Food Chem 57:637–644

Lindman B, Danielson I (1981) The definition of microemulsion. Colloid Surf 3:391–392

Liu SH, Campbell RA, Studens JA, Wagner RG (1996) Absorption and translocation of glyphosate in aspen (*Populus tremuloides* Michx.) as influenced by droplet size, droplet number, and herbicide concentration. Weed Sci 44:482–488

Mainx HG, Hofer P (2009) Alkylene oxide adducts of oligosaccharides. Patent WO 2009080215

Malec, AD, Figley, TM, Turpin, KL (2009) Ultra-high loading glyphosate concentrate. US Patent 20090318294

Marc J, Mulner-Lorillon O, Boulben S, Hureau D, Durand G, Belle R (2002) Pesticide Roundup® provokes cell division dysfunction at the level of CDK1/cyclin B activation. Chem Res Toxicol 15:326–331

Martinez TT, Brown K (1991) Oral and pulmonary toxicology of the surfactant used in Roundup® herbicide. Proc West Pharmacol Soc 34:43–46

Marvel JT, Brightwell BB, Suba L (1974) G 3780A surfactant: biodegradation, plant uptake, and ^{14}C-distribution. In: Report 321, Monsanto Company, St. Louis

May OL, Culpepper AS, Cerny RE, Coots CB, Corkern CB, Cothren JT, Croon KA, Ferreira KL, Hart JL, Hayes RM, Huber SA, Martens AB, McCloskey WB, Oppenhuizen ME, Patterson MG, Reynolds DB, Shappley ZW, Subramani J, Witten TK, York AC, Mullinix BG (2002) Transgenic cotton with improved resistance to glyphosate herbicide. Crop Sci 44:234–240

McAllister RS, Haderlie LC (1985) Translocation of ^{14}C-glyphosate and ^{14}C-CO$_2$-labeled photoassimilates in Canada thistle (*Cirsium arvense*). Weed Sci 33:153–159

Mercer GN (2007) A simple diffusion model of the effect of droplet size and spread. Area on foliar uptake of hydrophilic compounds. Pest Biochem Physiol 88:128–133

Minanaperez M, Gracia A, Lachaise J, Salager JL (1995) Solubilization of polar oils with extended surfactants. Colloid Surf A Physicochem Eng Asp 100:217–224

Morin F, Vera V, Nurit F, Tissut M, Marigo G (1997) Glyphosate uptake in *Catharanthus roseus* cells: role of a phosphate transporter. Pest Biochem Physiol 58:13–22

Muzik TJ (1976) Influence of environmental factors on toxicity to plants. In: Audus LJ (ed) Herbicides: physiology, biochemistry, ecology, 2nd edn. Academic, London, pp 203–247

Nadler-Hassar T, Goldshmidt A, Rubin B, Wolf S (2004) Glyphosate inhibits the translocation of green fluorescent protein and sucrose from a transgenic tobacco host to Cuscuta campestris Yunk. Planta 219:790–796

Nalewaja JD, Devilliers B, Matysiak R (1996) Surfactant and salt affect glyphosate retention and absorption. Weed Res 36:241–247

Nickel D, Föster T, von Rybinski W (1996) Physicochemical properties of alkyl polyglycosides. In: Hill K, Rybinski W, Stoll G (eds) Alkyl polyglucosides. VCH, Weinheim, pp 39–69

Odum J, Lefevre PA, Tittensor S, Paton D, Routledge EJ, Beresford NA, Sumpter JP, Ashby J (1997) The rodent uterotrophic assay: critical protocol features, studies with nonyl phenols, and comparison with a yeast estrogenicity assay. Regul Toxicol Pharmacol 25:176–188

Oparka KJ, Roberts AG (2001) Plasmodesmata. A not so open-and-shut case. Plant Physiol 125:123–126

Paganelli A, Gnazzo V, Acosta H, Lopez SL, Carrasco A (2010) Glyphosate-based herbicides produce teretogenic effects on vertebrates by impairing retinoic acid signaling. Chem Res Toxicol 23:1586–1595

Paveglio PL, Kilbride KM, Grue CE, Siemenstad CA, Fresh KL (1996) Use of Rodeo and X-77 spreader to control smooth cordgrass (Spartina alterniflora) in a southwestern Washington estuary: 1 environmental fate. Environ Toxicol Chem 15:961–968

Peixoto F (2005) Comparative effects of the Roundup® and glyphosate on mitochondrial oxidative phosphorylation. Chemosphere 61:1115–1122

Perkins MC, Roberts CJ, Briggs D, Davies MC, Friedmann A, Hart C, Bell G (2005) Macro and microthermal analysis of plant wax/surfactant interactions: plasticizing effects of two alcohol ethoxylated surfactants on an isolated cuticular wax and leaf model. Appl Surf Sci 243:158–165

Petracek PD, Fader RG, Knoche M, Bukovac MJ (1998) Surfactant-enhanced penetration of benzyladenine through isolated tomato fruit cuticular membranes. J Agric Food Chem 46:2346–2352

Pimentel D (1995) Amounts of pesticides reaching the target pests: environmental impacts and ethics. J Agric Environ Ethics 8:17–29

Pimentel D (1997) Techniques for reducing pesticide use. Wiley, New York

Pompeo MP, Mainx HG, Eskuchen R, Rosessing M, Abribat B (2005) APG Granules containing agrochemical active ingredients. US Patent 0,009,707

Pons M, Estelrich J (1996) Liposomes as an agrochemical tool: optimization of their production. Ind Crop Prod 5:203–208

Popp C, Burghardt M, Friedmann A, Riederer M (2005) Characterization of hydrophilic and lipophilic pathways of *Hedera helix* L. cuticular membranes: permeation of water and uncharged organic compounds. J Exp Bot 56:2797–2806

Price CE (1976) Penetration and translocation of herbicides and fungicides in plants. In: McFarlane NR (ed) Herbicides and fungicides-factors affecting their activity, vol 29, The chemical society special publication. Chemical Society, London, pp 42–66

Price CE (1983) The effect of environment on foliage uptake and translocation of herbicides. In: A.o.A. Biologists (ed) Aspects of applied biology 4: influence of environmental factors on herbicide performance and crop and weed biology, vol. 4, The Association of Applied Biologists, Warwick, pp 157–169

Prince LM (1977) Microemulsion. Academic, London

Rabea EI, Badawy MEI, Rogge TM, Stevens CV, Höfte M, Steurbaut W, Smagghe G (2005) Insecticidal and fungicidal activity of new synthesized chitosan derivatives. Pest Manag Sci 61:951–960

Ramsey RJL, Stephenson GR, Hall JC (2005) A review of effects of humidity, humectants, and surfactants composition on the absorption and efficacy of highly water-soluble herbicides. Pest Biochem Physiol 82:162–175

Reynhardt EC, Riederer M (1994) Structures and molecular dynamics of plant waxes. II Cuticular waxes from leaves of *Fagus sylvatica* L. and *Hordeum vulgare* L. Eur Biophys J 23:59–70

Richard EP Jr, Slife FW (1979) In vivo and in vitro characterization of the foliar entry of glyphosate in hemp dogbane *(Apocynum cannabinum)*. Weed Sci 27:426–433

Riechers DE (1992) Surfactant effects on the plasma membrane as a mode of action in promoting glyphosate phytotoxicity. M.Sc. thesis, University of Illinois, Urbana-Champaign

Riechers DE, Wax LM, Liebl RA, Bush DR (1994) Surfactant-increased glyphosate uptake into plasma membrane vesicles isolated from common lambsquarters leaves. Plant Physiol 105:1419–1425

Riechers DE, Wax LM, Liebl RA, Bullock DG (1995) Surfactant effects on glyphosate efficacy. Weed Technol 9:281–285

Riederer M, Markstädter C (1996) Cuticular waxes: a critical assessment of current knowledge. In: Kerstiens G (ed) Plant cuticles – an integrated functional approach. Bios Scientific, Oxford, pp 189–200

Riederer M, Schreiber L (2001) Protecting against water loss: analysis of the barrier properties of plant cuticles. J Exp Bot 52:2023–2032

Risbud MV, Bhonda RR (2000) Polyacrylamide-chitosan hydrogels: in vitro biocompatibility and sustained antibiotic release studies. Drug Deliv 7:69–75

Roberts J (2010) Helena Chemical Company, Presentation to EPA

Ryerse JS, Feng PCC, Sammons RD (2001) Endogenous fluorescence identifies dead cells in plants. Microsc Today 1:22–24

Saito H, Shinoda K (1967) The solubilization of hydrocarbons in aqueous solutions of nonionic surfactants. J Colloid Interface Sci 24:10–15

Santier S, Chamel A (1998) Reassessment of the role of cuticular waxes in the transfer of organic molecules through plant cuticles. Plant Physiol Biochem 36:225–231

Satchivi NM, Stoller EW, Wax LM, Briskin DP (2000a) A nonlinear dynamic simulation model for xenobiotic transport and whole plant allocation following foliar application I. Conceptual foundation for model development. Pestic Biochem Physiol 68:67–84

Satchivi NM, Stoller EW, Wax LM, Briskin DP (2000b) A nonlinear dynamic simulation model for xenobiotic transport and whole plant allocation following foliar application II. Model validation. Pestic Biochem Physiol 68:85–95

Satchivi NM, Stoller EW, Wax LM, Briskin DP (2001) A nonlinear dynamic simulation model for xenobiotic transport and whole plant allocation following foliar application III. Influence of chemical properties, plant characteristics, and environmental parameters on xenobiotic absorption and translocation. Pestic Biochem Physiol 71:77–87

Satchivi NM, Stoller EW, Wax LM, Briskin DP (2006) A nonlinear, dynamic, simulation model for transport, and whole plant allocation of systemic xenobiotics following foliar application IV. Physiochemical properties requirements for optimum absorption and translocation. Pestic Biochem Physiol 84:83–97

Schönherr J (2000) Calcium chloride penetrates plant cuticles via aqueous pores. Planta 212:112–118

Schönherr J (2002) A mechanistic analysis of penetration of glyphosate salts across astomatous cuticular membrane. Pest Manag Sci 58:343–351

Schönherr J, Schreiber L (2004) Size selectivity of aqueous pores in astomatous cuticular membranes isolated from Populus canescens (Aiton) Sm. leaves. Planta 219:405–411

Schönherr J, Baur P, Buchholz A (1999) Modelling foliar penetration: its role in optimising pesticide delivery. In: Brooks GT, Roberst TR (eds) Pesticide chemistry and bioscience. Royal Society of Chemistry, Cambridge, pp 134–151

Schönherr J, Baur P, Uhlig BA (2000) Rates of cuticular penetration of 1-naphthylacetic acid (NAA) as affected by adjuvants, temperature, humidity and water quality. Plant Growth Regul 31:61–74

Schreiber L (1995) A mechanistic approach towards surfactant/wax interactions: effects of octaethyleneglycolmonododecylether on sorption and diffusion of organic chemicals in reconstituted cuticular wax of barley leaves. Pestic Sci 45:1–11

Schreiber L (2006) Review of sorption and diffusion of lipophilic molecules in cuticular waxes and the effects of accelerators on the solute mobilities. J Exp Bot 57:2515–2523

Servizi JA, Gordon RW, Martens DW (1987) Acute toxicity of Garlon 4 and Roundup® herbicides to Salmon, Daphnia, and trout. Bull Environ Contam Toxicol 39:15–22

Sharma SD, Kirkwood RC, Whateley T (1996) Effect of nonionic nonylphenol surfactants on surface physiological properties, uptake and distribution of asulam and diflufenican. Weed Res 36:227–239

Sherrick SL, Holt HA, Hess FD (1986) Absorption and translocation of MON 0818 adjuvant in field bindweed *(Convolvulus amcnsis)*. Weed Sci 34:817–823

Soares A, Vijayram IA, Guieysse B, Murto M, Guieysse B, Mattiasson B (2005) Degradation of non-ionic surfactants under anaerobic conditions. In: Rittmann BE, van Loosdrecht MCM (eds) Third IWA leading-edge conference on water and wastewater treatment technologies. IWA Publishing, Sapporo

Solel Z, Edgington LV (1973) Transcuticular movement of fungicides. Phytopathology 63:505–510

Soto AM, Justicia H, Wray JW, Sonnenschein C (1991) P-Nonylphenol: an estrogenic xenobiotic released from "modified" polystyrene. Environ Health Perspect 92:167–173

Stephenson DO, Patterson MG, Faircloth WH, Lunsford JN (2004) Weed management with fomesafen preemergence in glyphosate-resistant cotton. Weed Technol 18:680–686

Stevens PJG, Bukovac MJ (1987) Studies on octylphenoxy surfactants. Part 1: effects of oxyethylene content on properties of potential relevance to foliar absorption. Pestic Sci 20:9–35

Stevens PJG, Baker EA, Anderson NH (1988) Factors affecting the foliar absorption and redistribution of pesticides. 2. Physicochemical properties of the active ingredient and the role of surfactant. Pestic Sci 24:31–53

Stewart WN (1993) Paleobotany and the evolution of plants, Secondth edn. Cambridge University Press, New York, 405

Stock D, Holloway PJ (1993) Possible mechanisms for surfactant-induced foliar uptake of agrochemicals. Pestic Sci 38:165–177

Stock D, Edgerton BM, Gaskin RE, Holloway PJ (1992) Surfactant enhanced foliar uptake of some organic compounds: interactions with two model polyoxyethylene aliphatic alcohols. Pestic Sci 34:233–242

Stock D, Holloway PJ, Grayson BT, Whitehouse P (1993) Development of a predictive uptake model to rationalise selection of polyoxyethylene surfactant adjuvants for foliage applied agrochemicals. Pestic Sci 37:233–245

Strey R (1996) Water – nonionic surfactant – systems, and the effect of additives. Berich Bunsen Gesell Phys Chem Chem Phys 100:182–189

Tabata A, Kashiwada S, Ohnishi Y, Ishikawa H, Miyamoto N, Itoh M, Magara Y (2001) Estrogenic influences of estradiol-17 beta, p-nonylphenol and bis-phenol-A on Japanese Medaka (*Oryzias latipes*) at detected environmental concentrations. Water Sci Technol 43:109–116

Tabira Y, Nakai M, Asai D, Yakabe Y, Tahara Y, Shinmyozu T, Noguchi M, Takatsuki M, Shimohigashi Y (1999) Structural requirements of para-alkylphenols to bind to estrogen receptor. Eur J Biochem 262:240–245

Tadros TF (1994) Surfactants in agrochemicals. Marcel Dekker, New York

Tadros TF (2005) Applications of surfactants in agrochemicals. In: Applied surfactants: principles and application. Wiley-VCH, Weinheim, pp 503–592

Tamura H, Knoche M, Bukovac MJ (2001) Evidence for surfactant solubilization of plant epicuticular wax. J Agric Food Chem 48:1809–1816

Thomas BA, Spicer RA (1987) The evolution and paleobiology of land plants, vol 2, Ecology, phytogeography and physiology series. Croom Helm, London, pp 309

Tice CM (2001) Selecting the right compounds for screening: does Lipinski's rule of 5 for pharmaceuticals apply to agrochemicals. Pest Manag Sci 57:3–16

Tilman D, Cassman KG, Matson PA, Naylor R, Polasky S (2002) Agricultural sustainability and intensive production practices. Nature 418:671–677

Tominack RL (2000) Herbicide formulations. J Toxicol Clin Toxicol 38:129–135

Trapp S (2004) Plant uptake and transport models for neutral and ionic chemicals. Environ Sci Pollut Res 11:33–39

Tsui MTK, Chu LM (2003) Aquatic toxicity of glyphosate-based formulations: comparison between different organisms and the effects of environmental factors. Chemosphere 52:1189–1197

Tu M, Hurd C, Randall JM (2003) Weed control methods handbook, The Nature Conservancy, Utah State University, Utah

Urano K, Saito M, Murata C (1984) Adsorption of surfactants on sediments. Chemosphere 12:293–300

van Ginkel CG, Stroo CA, Kroon AGM (1993) Biodegradability of ethoxylated fatty amines: detoxification through a central fission of these surfactants. Sci Total Environ 134:689–697

Wade BR, Riechers DE, Libel RA, Wax LM (1993) The plasma membrane as a barrier to herbicide penetration and site for adjuvant action. Pestic Sci 37:195–202

Wan Kim T, Amrhein N (1995) Glyphosate toxicity: long-term analysis of shikimic acid accumulation and chlorophyll degradation in tomato plants. Kor J Weed Sci 15:141–147

Wan MT, Watts RG, Moul DJ (1989) Effects of different dilution water types on the acute toxicity to juvenile Pacific salmon and rainbow trout of glyphosate and its formulated products. Bull Environ Contam Toxicol 43:378–385

Wang CJ, Liu ZQ (2007) Foliar uptake of pesticides – present status and future challenge. Pest Biochem and Physiol 87:1–8

Wang L, Li X, Zhang G, Dong J, Eastoe J (2007) Oil-in-water nanoemulsions for pesticide formulations. J Colloid Interface Sci 314:230–235

White R, Jobling S, Hoare SA, Sumpter JP, Parker MG (1994) Environmentally persistent alkylphenolic compounds are estrogenic. Endocrinology 135:175–182

Williams GM, Kroes R, Munro IC (2000) Safety evaluation and risk assessment of the herbicide Roundup® and its active ingredient, glyphosate, for humans. Regul Toxicol Pharmacol 31: 117–165

Wills GD, McWhorter CG (1988) Absorption and translocation of herbicides effect of environment, adjuvants, and inorganic salts, pesticide formulations. In: Chapter 8, ACS symposium series, Vol 371, American Chemical Society, Washington, pp 90–101

Woodburn A (2000) Glyphosate: production, pricing and use worldwide. Pest Manage Sci 56:309–312

Wyrill JB, Burnside OC (1976) Absorption, translocation, and metabolism of 2,4-D and glyphosate in common milkweed and hemp dogbane. Weed Sci 24:557–566

Yoshihara K, Ohshima H, Momozawa N, Sakai H, Abe M (1995) Binding constants of symmetric or antisymmetric electrolytes and aggregation numbers of oil-in-water type microemulsions with a nonionic surfactant. Langmuir 11:2979–2984

Zabkiewicz JA (2000) Adjuvants and herbicidal efficacy – present status and future prospects. Weed Res 40:139–149

Zabkiewicz JA (2003) Foliar interactions and uptake of agrichemical formulations – present limits and future potential. In: Voss G, Ramos G (eds) Chemistry of crop protection. Wiley VCH, Weinheim, pp 237–251

Zabkiewicz JA (2007) Spray formulation efficacy – holistic and futuristic perspectives. Crop Prot 26:312–319

Zhang C, Ping QN, Zhang H, Shen J (2003) Preparation of N-alkyl-O-sulfate chitosan derivatives and micellar solubilization of taxol. Carbohyd Polym 54:137–141

Zhang C, Qu GW, Sun YJ, Wu XL, Yao Z, Guo QL, Ding Q, Yuan S, Shen Z, Ping Q, Zhou H (2008) Pharmacokinetics, biodistribution, efficacy and safety of N-octyl-O-sulphate chitosan micelles loaded with paclitaxel. Biomaterials 29:1233–1241

Zhu L, Chen B, Tao S (2004) Sorption behavior of polycyclic aromatic hydrocarbons in soil-water system containing nonionic surfactant. Environ Eng Sci 21:263–272

Zhu H, Yu Y, Ozkan HE, Derksen RC, Krause CR (2008) Evaporation and wetted area of single droplets on waxy and hairy leaf surfaces. Commun Agric Appl Biol Sci 73:711–718

Zoller U (2009) Handbook of detergents. Part F: production, vol 142, Surfactant science series. Taylor and Francis Group, New York