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Formulation technology: key parameters for food safety with respect to agrochemicals use in crop protection

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A B S T R A C T

A very small fraction of all applied pesticides is directly involved in the pesticidal mechanism. This implies that most of the applied pesticides find their way as 'residue' in food chains where they undergo concentration and produce potential, long term, adverse health effects. Pesticides in developing countries in Asia and Pacific region are mainly available as dust, wettable powder, emulsifiable concentrates, solutions, etc. These types of formulations are regarded now as ‘conventional’, ‘old technology’ or ‘classical’ or ‘traditional’ because of their increased in dose rate or repeated applications to get desired bioefficacy which lead to accumulation of pesticide residues in food commodities along with environmental pollution. Conventional formulations, because of their characteristics i.e. dustiness and use of volatile organic solvents in their preparation maximize several problems like health hazards and environmental pollution etc. With the increasing awareness of toxic effects of conventional formulations, there is a significant trend towards switching over from such pesticide formulations using petroleum and organic solvent based constituents to user and environment friendly water based formulations. These formulations not only replace toxic, non-degradable ingredients/adjuvants of the conventional formulations but also increase the bio-efficacy of the products through incorporating latest technologies including size reduction (WP to SC, SL to ME), increased coverage of applied surface area (EC to ME/Nano-formulations), reduced wastage (Dust/WP to Controlled Release Formulations) and dose rates of same pesticides applied to improve food quality with minimum pesticide residues.

Keywords: Conventional, agrochemicals, toxic, environment, new-generation, adjuvant

Introduction

If the credits of pesticides include enhanced economic potential in terms of increased production of food and fibre, and amelioration of vector-borne diseases, then their debits have resulted in serious health implications to man and his environment. It has been estimated that the world-wide deaths and chronic illnesses due to pesticide poisoning number about 1 million per year. Ideally a pesticide must be lethal to the targeted pests, but not to non-target species, including man. Unfortunately, this is not so the controversy of use and abuse of pesticides has surfaced (Mathur 1999). The rampant use of these chemicals, under the adage, ‘if little is good, a lot more will be better’ has played havoc with human and other life forms. Applied conventional agrochemicals (90%) never reach their objective to produce desired biological response at the present time and in precise quantities due to non-specific and periodic applications. This implies that most of the applied pesticides find their way as 'residue' in food chains where they undergo concentration and exert potential, long term; adverse health effects (Gupta 2004). Their concentration in food samples varies greatly not only from region to region and year to year but also from one specific food item to another within the same food group. Perusal of the residue data on pesticides in samples of fruits, vegetables, cereals, pulses, grains, wheat flour, oils, eggs, meat, fish, poultry, bovine milk, butter and cheese in India indicates their presence in sizeable amounts (Geisler *et al.* 2004).

Pesticides in developing countries in Asia and Pacific region are mainly available as dust, wettable powder, emulsifiable concentrates, solutions, etc. These types of formulations are regarded now as in 'conventional', 'old technology' or 'classical' or 'traditional' because of their increased dose rate or repeated applications to get desired bioefficacy. These higher doses and repeated applications lead to accumulate pesticide residues in food commodities along with environmental pollution. Conventional formulations, because of their characteristics i.e. dustiness and use of volatile organic compounds (VOCs) in their preparation maximize several problems like pesticide residues in food and finished products etc. The economic impact of pesticides in non-target species (including humans) has been estimated at approximately $8 billion annually in developing countries. Because of the huge benefits which man accrues from pesticides, these chemicals provide best opportunity to those who juggle with the risk-benefit equation. With the increasing awareness of toxic effects of conventional formulations, there is a significant trend towards switching over from such pesticide formulations using petroleum and organic solvent based constituents to user and environment friendly water based pesticide formulations (Green *et al.* 2007). The developed world has progressed substantially in this regard to develop eco-friendly formulations which are safer to food and the environment. These formulations would not only replace toxic, non-degradable ingredients/adjuvants of the conventional formulations but also increase the bio-efficacy of the products through incorporating latest technologies including size reduction (Wettable Powder to Suspension Concentrate, Soluble Liquid to Microemulsion), increased coverage of applied surface area (EC to ME/Nano-formulations), reduced wastage (Dust/WP to Controlled Release Formulations) and dose rates of applied same pesticides to improve food quality with minimum pesticide residues. Suspension Concentrates, Water Dispersible Granules, Emulsion in Water, Micro-emulsion, Combination Formulations, Effervescent Tablets, Floating Tablets, seed treatment formulations etc. are some of the formulation types that come under this category of safer formulations for the production of safe and clean food (Knowles 1998).

Pesticide Formulation Process

The active ingredients in pesticide products come from many sources. Some, such as nicotine, pyrethrum, and rotenone, are extracted from plants. Others have a mineral origin, while a few are derived from microbes. However, the vast majority of active ingredients are synthesized (man-made) in the laboratory.

These synthetic active ingredients may have been designed by an organic chemist or discovered through a screening process of chemicals generated by various industries. Regardless of their source, pesticide active ingredients have different solubilities. Some dissolve readily in water, others only in oils. Some active ingredients may be relatively insoluble in either water or oils. These different solubility characteristics, coupled with the intended use of the pesticide, in large measure define the types of formulations in which the active ingredient may be delivered. It is preferable from the manufacturer's perspective to use the active ingredient in original form, whenever possible (e.g., a water soluble active ingredient formulated as a soluble liquid). When this is not feasible; it may become necessary to alter the active ingredient in order to change its solubility characteristics. This is done, obviously, in a manner that does not detract from the pesticidal properties of the active ingredient. Usually, an active ingredient is combined with appropriate inert materials i.e. formulation or finished product prior to packaging (Tadross 1995). A brief review of some basic chemistry terminology should prove helpful in understanding differences among the various types of formulations.

Formulation Selection Considerations

The importance of formulation type is generally over looked. A well-considered decision to use the most appropriate formulation for a given application requires detailed analysis of the following factors (Agrow Report 2001).

Applicator safety

Different formulations present various degrees of hazard to the applicator. Some products are easily inhaled, while others can penetrate skin or cause injury when splashed in the eyes.

Environmental concerns

Special precautions need to be taken with formulations that are prone to drift in air or move off target into water. Wild life can also be affected to varying degrees by different formulations. Birds may be attracted by granules, and fish or aquatic invertebrates can prove especially sensitive to specific pesticide formulations.

Pest biology

The growth habits and survival strategies of a pest generally determine which formulation provides optimum contact between the active ingredient and the pest.

Available equipment

Some pesticide formulations require specialized handling equipment. This includes application equipment, safety equipment, and spill control equipment.

Surfaces to be protected

Applicators must be aware that certain formulations can stain fabrics, discolor container, dissolve plastic, or burn foliage.

Cost

Product prices may vary substantially, based on the ingredients used and the complexity of delivering active ingredients in specific formulations.

Individuals such as commercial pest control technicians or farm workers who may not be involved in the selection process but are responsible for the actual application also should be very aware of the type of formulation they are using. As stated, formulation type can have an impact on hazards to human health and the environment. In attention to the type of formulation being used could mean the difference between a routine application and one that is the source of environmental contamination—or worse, a serious human exposure (Gupta 2004).

Formulation types of Agrochemicals

Different types of formulations of agrochemicals can be identified depending on the application, customer acceptability and regional market requirements. At present, most agrochemical companies attempt to formulate a product in a form that can be accepted globally (Mulqueen 2003). This presents a challenge to the formulation scientists who not only needs to understand the basic and fundamental principles in such formulation types, but also should be able to produce formulations that can be applied worldwide.

The first three classes mentioned in the table 1, may be considered as 'conventional/ classical/old' formulation types. The latter classes have been introduced more recently as fall in the category of environmental and user friendly pesticide formulations.

Drawbacks of conventional formulations

Granules (GR)

Granular pesticide formulations are distinguished from powder formulations according to mesh size. It is generally accepted that a granular formulation is a product with a size range from 16-60 British Standard BS mesh (250-1000 microns) with at least 90% of the granules within the specified mesh size range. Granules are, therefore, the largest of the solid pesticide formulations (apart from tablets) and their large size virtually eliminates drift leading to much less loss of pesticide than with powder and liquid formulations. Granular formulations are often used as pre-emergence herbicides or as soil insecticides for direct broadcasting to the field. They are also applied for "in-furrow" use, especially for insecticides. The active ingredient concentration is usually from 1-40% and the granules should be free

Table 1.
Types of Agrochemical Formulations

Type	Abbreviation	Description
Emulsifiable Concentrate	EC	Oil solution of active ingredient plus emulsifiers
Wettable Powder	WP	Solid active plus filler plus dispersing & wetting agents
Solution	SL	Solution of active ingredient, mostly in water miscible solvents
Suspension Concentrate	SC	Solid/liquid dispersion (suspension)
Emulsion (Concentrated)	EW	Oil-in-water emulsion
Suspoemulsion	SE	Mixture of suspension and emulsion
Water Dispersible Granule	WG	Active plus filler plus dispersing agent that is readily dispersed into water

flowing and should disintegrate in the soil to release the active ingredient. Many cheap absorbent carriers are used for granule formulations and they may be of mineral or vegetable origin. Mineral based carriers may have acid sites on the particle surfaces which could cause decomposition of the active ingredient. This may be overcome by adding 1-2% of a stabilizer such as deoxidized linseed oil. The mechanical strength of extruded and uncalcined carrier preformed granules is generally good, while botanical carriers are very resistant to mechanical breakdown (Agrow Report 1995). Granular products are very important in Japan and other Asian countries for the application of insecticides to paddy rice. Granule formulations are effective because they sink through the water to the bottom of the rice plants and slowly disintegrate to release the active ingredients. In general, there is a question mark over the future of granules for a number of reasons mainly that they tend to be low strength products application and the current trend for herbicides is to move towards post emergence.

Wettable Powders (WP)

Wettable powders are finely-divided solid pesticide formulations which are applied after dilution and as a suspension in water. They have been used for many years and are second only to emulsifiable concentrates in terms of the total volume of products produced globally. Wettable powder formulations are usually made from solid active ingredients which are suitable for fine grinding through a hammer or pin type mill or a fluid energy micronizer. The powders contain dry surfactants as powder wetting and dispersing agents and inert carriers or fillers. Wettable powders may contain more than 50% active ingredient. The upper limit of active ingredient depends on the amount of inert filler materials required to prevent the active ingredient particles fusing together during the grinding process. This is influenced by the melting point of the active ingredient. Inert filler is also needed to prevent the formulated product from caking or aggregating during storage. Wettable powders contain many particles of less than 5 microns and all the particles should pass through a 45micron screen (350 BS Mesh or 325 ASTM Mesh). These particles are larger than the droplets produced by emulsifiable concentrate formulations. It is this factor, coupled with the lack of solvent, which gives WP's lower biological activity than most liquid formulations. However, this also makes them less likely to cause phytotoxicity to crops. Powder formulations are made by blending the active ingredient with surfactant wetting and dispersing agents and inert fillers, followed by grinding to the required particle size. The wetting agent lowers the interfacial tension between the solid particles and water, with the result that the powder wets and mixes with water in the spray tank much more easily. The dispersing agent prevents the particles in the spray tank from flocculating or aggregating together. This ensures that the particles remain suspended in water during the spraying operation. This formulation has some disadvantages like difficult to mix in spray tanks, poor compatibility with other formulations, tank mix wetter may be needed, dust hazard during manufacture and application etc.

Wettable powders can present serious health and safety issues for manufacturers because of their dustiness, which can give rise to operator inhalation and skin and eye irritation problems if stringent safety precautions are not taken. The grinding and mixing of dusty powders can also give dust explosion hazards with sensitive materials. For these reasons, and because of their low-tech image and also their dustiness during application, wettable powders are gradually being superseded by suspension concentrates or water dispersible granules. In some cases, wettable powders have been given a new lease of life by the introduction of water soluble sachets which overcome the dust handling hazard problems (Gupta 2004). However, this type of packaging is not without its problems, and care must be taken to ensure compatibility between the product and the water soluble film (usually PVA). The sachets range from a few grams up to about 25 kg and must be over packed with polythene and/or aluminium film. The fact that water soluble packs represent a unit dose can be inconvenient for large scale intensive farming.

Emulsifiable Concentrates (EC)

Emulsifiable concentrates are popular for active ingredients which are very soluble in non-polar solvents. They are formulated by dissolving the active ingredient with emulsifying surfactants in an organic solvent. Originally, xylene was used as a solvent, and still is used in some developing countries, but this has now been replaced by safer solvents with higher flash points. The formulations are generally stable for at least two to three years at a wide range of storage temperatures from -10 ^{0}C to +50 ^{0}C. EC formulations are easy to use and, when diluted in water, should give a stable “milky” emulsion with very little creaming and no oil separation. EC formulations must also be compatible with spray tank water covering a range of water hardness from very soft water up to about 1,000 ppm of hardness. Emulsifiable concentrate formulations comprise the biggest volume of all pesticide formulations representing about 40% in terms of global volume usage (Knowles 2008). Surfactant emulsifier blends are added to these formulations to ensure spontaneous emulsification into water in the spray tank. Surfactant suppliers provide advice on the selection of a "balanced pair" emulsifier blend to ensure good emulsion stability after dilution in water of varying degrees of water hardness. Emulsion droplets up to about 10 microns are formed when the product is diluted in water in the spray tank. No of drawbacks like emulsion stability problems after dilution, phytotoxicity to crops, dermal toxicity of active ingredient, possible fire hazard and solvent corrosiveness to plastics and rubbers in during spray application decreasing the popularity of this formulation.

Despite the trend to move away from petroleum-based solvent formulations towards water based or solid formulations, EC formulations are still very popular, especially in developing countries in Asia and South America. Furthermore, in some cases the presence of a solvent is necessary to impart acceptable biological activity for some active ingredients. The toxicity of alkyphenolethoxylate surfactants (APE's), such as nonylphenolethoxylates (NPE's), has been reviewed in the last few years because of growing concern regarding the potential endocrine modifying properties of these surfactants or their metabolites. This was recognized at the North Sea Ministerial Conference in 1995, where it was decided to expand the definition of "hazardous substances" to include those which have adverse effects on the endocrine system. Nonylphenol and nonylphenolethoxylates and related substances were specifically mentioned as substances that should be substituted by less hazardous alternatives.

The Paris Commission (PARCOM) agreed, in its Recommendation 92/8, that all uses of NPE's and similar substances which may be discharged to sewers or surface water should be examined with a view to reducing their usage. It was recommended that the use of NPE's in domestic detergents should be phased out by 1995 and that their use in industrial detergents should be phased out by 2000. There are proposals in Scandinavian countries to phase out APE's from all applications, and Sweden has stopped giving registration to formulations containing APE's. Denmark also has a policy to phase out these additives by 2000. The ECPA (European Crop Protection Agency) and EAA (European Adjuvant Agency) support the phasing out of APE's from pesticide formulations and adjuvants, and agrochemical industry has now stopped developing new formulations containing APE's. Consequently, alternate relatively safe such as alcohol ethoxylates are being used, particularly for emulsifiable concentrates. There is increasing interest in the effect of surfactants on toxicity to mammals and fish (Hewein International 2000). These effects can be due to the inherent toxicity of the surfactant itself or to the enhancing effect that the surfactant may have on the toxicity of the active ingredient. Formulators who are moving away from nonylphenolethoxylates are looking to replace them with products that carry no hazard label and have an environmental profile which meets current and likely future regulations. Monobranched alcohol ethoxylates (MBA) are a new class of non-ionic surfactants that have been shown to be particularly suitable for NPE replacement in EC formulations. This range of speciality alcohol ethoxylates ranging from C_{11} to C_{15} alcohols does not carry a hazard classification.

Soluble Liquid (SL)

A soluble liquid is a clear solution to be applied as a solution after dilution in water. Soluble liquids are based on either water or a solvent mixture which is completely miscible in water. Solution liquid are the simplest of all the formulation types and merely require dilution into water in the spray tank. However, the number of pesticides which can be formulated in this way is limited by two factors, the solubility and hydrolytic stability of the active ingredient in water. The solubility factor limits these formulations to salts of active acids or, in the case of paraquat and diquat, of active bases. The active acids used as active ingredients include 2:4-D, MCPA, dicamba and glyphosate and the formation of salts is usually achieved by reacting these acids with neutralizing bases to form sodium, potassium or amine salts, but in the case of glyphosate in its isopropylamine or trimesium salts (Zabkiewicz 2000). Water based solution concentrate formulations are hydrophilic after spraying onto crops and, therefore, often contain a surfactant to assist wetting onto the leaf surface. These wetting agents are generally of the non-ionic type, such as nonylphenolethoxylate. They may also contain antifreeze and antifoam agents. Nonylphenolethoxylates are now suspected of having endocrine modifying properties from metabolites in effluent water which may leach into waterways or even into drinking water. Surfactant suppliers have now developed alternative surfactants, such as alcohol ethoxylates, to replace nonylphenolsurfactants. It is sometimes necessary to use a water-miscible solvent to increase the concentration of active ingredient in the formulation. For this purpose, high molecular weight glycol ethers such as diethylene glycol (2, 2'-dihydroxy diethylether) are preferred to methanol or acetone because of their higher flash points. SL formulations also have some drawbacks like often requires surfactant wetters for good wetting/spreading on leaves, poor low temperature stability, may hydrolyze active ingredients and corrosive to metals etc.

Trends towards Safer Formulation Technologies

However, there has been a dramatic shift from WP formulations to WG, from EC to EW. SCs have also increased in popularity due to their environmental advantages, being water based, and their ease of application (spontaneous dispersion on dilution into water). In all the above formulations, considerable attention has been paid in recent years to achieve a number of objectives namely broader formulation inerts, solvent reduction and safer solvent selection, safer surfactant components with low toxicity, low skin irritation and enhanced biodegradability, long term physical and chemical stability, enhancement of bioefficacy by incorporation of adjuvants, controlled and sustained release formulations and compatibility of various formulations in tank mixes. These challenges require good knowledge of colloid and surface science as well as the key factors involved in formulating complex systems. In this review, some of the recent advances in agrochemical formulation technology will be discussed in the six-main areas like water based dispersion technology, improved dry product technology, gel technologies for delivery in water-soluble packs, controlled release technologies for improved product performance, combined/mixed formulation technology and nanotechnology-based pesticides due to size and surface characteristics (Hiromoto 2007).

Water based Dispersion Technology

Suspension Concentrates (SC)

Suspension concentrate technology has been increasingly applied to the formulation of many solid crystalline pesticides since the early 1970's (Mulqueen 2003). Pesticide particles maybe suspended in an oil phase, but it is much more usual for suspension concentrates to be dispersions in water. Considerable attention has been given in recent years to the production of aqueous suspension concentrates by a high energy wet grinding processes such as bead milling. The use of surfactants as wetting and dispersing agents has also led to a great deal of research on the colloidal and surface chemistry aspects of dispersion and stabilization of solid/liquid dispersions. Water-based suspension concentrate formulations offer many advantages such as: high concentration of insoluble active ingredients, ease of handling and application, safety to the operator and environment, relatively low cost and enable water-soluble adjuvants to be built-in for enhanced biological activity.

Farmers generally prefer suspension concentrates to wettable powders because they are non-dusty and easy to measure and pour into the spray tank. However, there are some disadvantages, notably the need to produce formulations which do not separate badly on storage, and also to protect the product from freezing which may cause aggregation of the particles. In most cases, suspension concentrates are made by dispersing the active ingredient powder in an aqueous solution of a wetting and dispersing agent using a high shear mixer to give a concentrated premix, followed by a wet grinding process in a bead mill to give a particle size distribution in the range 1–10 microns. The wetting/dispersing agent aids the wetting of the powder into water and the breaking of aggregates, agglomerates and single crystals into smaller particles. In addition, the surfactant which becomes adsorbed onto the freshly formed particle surface during the grinding process should prevent re-aggregation of the small particles and should ensure colloidal stability of the dispersion. Typical wetting/dispersing agents used in suspension concentrate formulations are: sodium lingo sulphonates, sodium naphthalene sulphonate formaldehyde condensates, aliphatic alcohol ethoxylates, tristyryl phenol ethoxylates and esters and ethylene oxide/propylene oxide block copolymers etc.

More recently available are polymeric surfactants, such as ''comb'' surfactants, which adsorb strongly on particle surfaces and may give considerably improved stabilization of suspension concentrates for long term storage. The anti-settling agent is added to increase viscosity and build up a three dimensional network structure to prevent separation of particles during long term storage. The anti-settling agent is usually swelling clay such as betonies (sodium montmorillonite) and may be mixed with water soluble polymers to give synergistic rheological effects. The water soluble polymers are often cellulose derivatives, natural gums or other types of polysaccharides, such as xanthan gum, and they are generally susceptible to microbial attack. For this reason, preservatives are usually added to suspension concentrate formulations to prevent degradation of the anti-settling agent so that long term stability of the product is not impaired. A great deal of research has been carried out using rheological techniques to measure the forces acting between particles and polymers to enable storage stability to be predicted (Green *et al.* 2007). However, it is still necessary to carry out long term storage tests over a range of temperatures to ensure that the particles do not aggregate or separate irreversibly under normal storage conditions in the sales pack. Examples of SC formulations are Fipronil 5SC, Sulphur 52SC, Hexaconazole 10SC, Carbendazim 50SC etc.

O/W Emulsions (EW)

Oil-in-water emulsions are now receiving considerable attention because of the need to reduce or eliminate volatile organic compounds (VOCs) for safer handling. Because they are water based, oil-in-water emulsions can have significant advantages over emulsifiable concentrates in terms of cost and safety in manufacture, transportation and use. Key is that the active ingredient must have very low water solubility to avoid crystallization issues. A solid active may be dissolved in a water–immiscible solvent. Oil-in-water emulsions (EWs) consist of a dispersion of oil droplets in a continuous aqueous medium. Such EW or SE products tend to have lower skin and eye toxicity ratings than the corresponding EC products as well as higher flash points and better compatibility with high-density polyethylene (HDPE) containers (Ware *et al.* 2004). However, they require careful selection of surfactant emulsifiers to prevent flocculation, creaming and coalescence of the oil droplets. Non-ionic surfactants block copolymers and other polymeric surfactants are now being used to produce stable emulsions. In the case of non-ionic surfactants it is sometimes useful to combine a low and a high HLB surfactant to give an emulsifier mixture with an average HLB of 11 –16 for optimum emulsion stability (Tadros 1995). Droplet size is also a good indicator of stability and should be below 2 microns (volume mean diameter VMD). The emulsions are usually thickened with polysaccharides such as xanthan gum to prevent separation of the oil droplets. Sometimes polymers such as polyvinyl alcohol are used as both emulsifier and thickener/stabilizer. EWs, unlike ECs in the undiluted state, are only stable in the kinetic sense. This is because the system is inherently thermodynamically unstable and can only be formed non-spontaneously. Examples are Butachlor 50 EW, Cyfluthrin 5 EW, Tricontanol 0.1 EW etc.

Suspo-emulsions (SE)

Mixed combination formulations are becoming more popular because of their convenience, they ensure that the farmer applies the correct amount of each component pesticide and overcome problems of tank mix incompatibility. If one active ingredient is a solid and the other is a liquid, it is necessary to produce a suspo-emulsion formulation, which consists of three phases: namely solid dispersed particles, liquid oil droplets and continuous phase, usually water.

Suspo-emulsions can, therefore, is considered to be mixtures of suspension concentrates and oil-in-water emulsions with added surfactants to prevent flocculation and thickeners to prevent separation of the dispersed phases. Surfactants used as dispersing agents for the solid phase are similar to those already mentioned for suspension concentrates. Emulsifiers for the oily liquid phase are similar to those used for oil-in-water emulsions. As these formulations are aqueous based and generally thickened with polysaccharides, it is necessary to add a preservative to prevent degradation of the thickener. Careful selection of the appropriate dispersing and emulsifying agents is necessary to overcome the problem of hetero-flocculation between the solid particles and the oil droplets and extensive storage testing of these formulations is necessary (Tadros 1995). SE formulation can be exampled as: Fenpropimorph 24.5 + Epoxiconazole 8.2 SE (Not registered in India)

Microemulsions (ME)

Microemulsions are thermodynamically stable transparent dispersions of two immiscible liquids and are stable over a wide temperature range. They have a very fine droplet size of less than 0.05 microns (50 nanometers) and consist of three components, namely: oily liquid or solid dissolved in organic solvent, water and surfactant/co-surfactant system.

These components form a single phase containing relatively large 'swollen micelles' in which the non-aqueous phase of the active ingredient and solvent are dissolved or solubilised by the surfactant system. In the preparation of microemulsions two different types of surfactants are needed; one water soluble and one oil soluble. The water soluble surfactant is usually anionic or non-ionic with a very high HLB value, and the hydro-phobic part of the surfactant molecule should match the oil. The co-surfactant should be oil soluble and should have a very low HLB value, for example hexanol. The total concentration of surfactants for a microemulsion can be as high as 10 –30% or more, compared with about 5% for a typical o/w emulsion (Tadros 1995). Microemulsions have relatively low active ingredient concentrations, but the high surfactant content and solubilisation of the active ingredient may give rise to enhanced biological activity. Examples of ME formulations are: Neemazal 30 MEC, Pyrithiobac Na 5.4 + Quizalofop-P-Ethyl 10.6 ME etc

Multiple Emulsions

Another class of emulsion is the multiple emulsions, which can be water-in-oil-in-water (W/O/W) or oil-in-water-in-oil (O/W/O). These are complex formulations which require very careful selection of surfactant emulsifiers and stabilizers to overcome physical instability problems. Multiple emulsions are still in the research phase and could be of interest to reduce the oral toxicity of an active ingredient by restricting it to the primary internal emulsion droplet phase. However, because of the need to form a second emulsion phase, the final product must be of low active ingredient content.

New Dry product Technology

Water Dispersible Granules (WG)

Water dispersible granules, or dry flowables as they are sometimes known, are a relatively new type of formulation and are being developed as safer and more commercially attractive alternatives to wettable powders and suspension concentrates. They are becoming more popular because of their convenience in packaging and use, being non-dusty, free-flowing granules which should disperse quickly when added to water in the spray tank. They therefore represent a technological improvement over wettable powders and imitate liquids in their handling characteristics. They can be packed into paper bags or cartons with the minimum of contamination and pack disposal problems. The technology for water dispersible granules is rather complex because they can be formulated using various processing techniques, but in each case the resultant product must redisperse in the spray tank to give the same particle size distribution as the original powder or suspension from which it is made. The most important processes for producing water dispersible granules are pan granulation, high speed mixing agglomeration, extrusion granulation, fluid bed spray granulation and spray drying.

Regional availability originally influenced the choice of granulation and drying technique. The producers associated with the pharmaceutical industry allowed the initial investigation of spray drying, fluidized-bed granulation and some extrusion techniques for agricultural formulation (Knowles 1998). Several factors, such as the physico-chemical properties of the active ingredient and additives, need to be considered when deciding upon which process to use. These factors and the various processing techniques used to make water dispersible granules determine the main properties of the final product in terms of granule shape and size, degree of dustiness and ease of dispersion into water. It can be seen that skill and experience are required to obtain satisfactory products by each type of process. Pan granulation has been used for many years particularly in the USA, but can be a dusty operation and is now much less popular. Fluid bed spray granulation and spray drying involve the filtration and containment of large volumes of hot air. Furthermore, the plants tend to be rather large and expensive. Dry compaction gives a hard product with very poor dispersion properties in water unless effervescing agents are added to the formulation. Extrusion granulation is one of the safest, most versatile and economical process and is probably the most favoured process used by agrochemical companies at the present time, followed closely by fluid bed spray granulation. The trends for WDG extrusion are the incorporation of bio-efficacy enhancing adjuvant into the granule alone with other additives to improve physical performance or process ability: stability, compatibility with ECs and process enhancing lubricants. Often each of these traits must be specifically developed for the specific pesticide and concentration.

The dispersion time in water is a very important property and to ensure that no problems occur in the spray tank it is necessary for all the granules to disperse completely within two minutes in varying degrees of water temperature and hardness. This can be achieved by optimizing the formulation additives and process parameters (Agrow Report 2001). Water dispersible granules usually contain a wetting agent and a dispersing agent in the same way as a wettable powder or a suspension concentrate. Improved dispersants for difficult WDG formulations have been developed. Research has demonstrated that combination dispersants can improve formulation suspensibility, particularly when the dispersants are co-mixed before use. Surfactant companies are collaborating in this area when each party has unique chemistry. Dispersant blends, in a soluble liquid or spray dried form, may synergistically improve performance in suspension tests. The selection of dispersant components depends upon the nature of the other formulation components. Some dispersants may enhance the rate of wetting and granule breakdown rate; others will enhance suspension via steric stabilization, while others can overcome the challenge to suspend high silica-containing formulations, such as with low-melt active ingredients. They may also contain water soluble salt to act as a disintegrant in the spray tank. The remainder of the formulation is usually water soluble or a water dispersible filler. For instance, we can give examples of Mancozeb 75 WG, Endosulfan 50 WG, Captan 83 WG, Cypermethrin 40 WG, Thiomethaxam 25 WG, Deltamethrin 25 WG etc.

Effervescent Tablets (WT)

The invention relates to an effervescent tablet utilizing the acid-alkali neutralizing reaction to produce self-dispersion of pesticides. When the effervescent tablet of the invention is dissolved in water, the bubbles of carbon dioxide can be rapidly released and stable suspension can be obtained; and the acid-alkali neutralizing reaction can be utilized to self-mix of tablets in water. The effervescent tablet has high stability, convenient operation, high dissolving speed and the raw materials of the effervescent tablet are safe and non-toxic, thus avoiding the secondary pollution of fruits and vegetables. Example of effervescent tablet formulation is Deltamethrin 12.5% + Piperonyl Butoxide 12.5% WT

Novel Gel Technology

Packaging oil based products as gels has become an interesting method of reducing packaging waste on selected formulations. Gel formulations are innovative products, which can be described as thickened ECs packed in water-soluble bags. The viscosity is increased with thickeners, the final gel viscosity being a compromise between the transport stability in the water-soluble bag and the dispersibility in water. This formulation approach is to resist leakage from the pinhole imperfections of the water-soluble bags. This concept offers the crop protection market with a new form of a product packaging combination. The first fungicide formulated as a gel is propiconazole in France in 1991.Gel products offer many benefits that are highly appreciated by farmers. The premeasured doses in water soluble bags offer advantages in ease of handling and increased user safety while the outer packaging is sometimes considered as non-contaminated with product and, therefore, more easily disposed of. An improved method of producing gelled products has been identified. In this method, non-aqueous liquid formulations are gelled and then and suitably packaged within polyvinyl alcohol film as water-soluble sachets or bags. Gelation of liquid formulations can be brought about by thickening agents such as polyacrylic acids, xanthan gum, silicas, clays, surfactants and combinations thereof. Syngenta found that gelation could be brought on by mixing a liquid EC formulation with high surface-area silica in combination with an ethoxylated non-ionic emulsifier. They found that gelation occurs at ambient temperature, gel rheology is highly controllable and the process is versatile. A water soluble bag containing such gels which on addition to water, releases its contents within 1 min, the gel disperses homogeneously and the sachet film dissolves completely within 3 min. Water-based gels that have stable formulations of hydrolytically unstable sulfonylurea herbicides have also been developed. Gels containing sulfonylurea and co-pesticides add a new dimension to delivery of compounds which rapidly degrades. For example: Imidacloprid 2.5 Gel formulation.

Controlled Release Technologies for Improved Product Performance

Microencapsulation / Capsule Suspensions (CS)

The polymer membrane, or microencapsulation technique, has become popular in recent years (Beestman 2003). A well-known method of microencapsulation uses the principle of interfacial polymerization. In this process the active ingredient, usually a liquid or low melting waxy solid, is dissolved in an organic solvent, such as the C9 and C10 used for emulsifiable concentrates. An oil-soluble monomer such as toluene diisocyanate (TDI) is dissolved in the solvent mixture. A fine emulsion of the oil phase in water is made by high shear mixing with an aqueous solution of an emulsifier and a reactive amine, such as ethylene diamine. An emulsion with droplets of 5–30m is formed, and polymerization between the isocyanate and the amine occurs at the oil/water interface giving a polyurea membrane around each droplet. Alternatively the interfacial polymerization process may be carried out by allowing the isocyanate to react with water at the interface to form an amine in situ, which then reacts with more isocyanate to form a polyurea membrane. The rate of release of the active ingredient can be controlled by adjusting the droplet size, the thickness of the polymer membrane and the degree of cross-linking or porosity of the polymer. The rate of release of the pesticide is, therefore, a diffusion controlled process (Fernandez 2007).

Microcapsule suspensions need to be stabilized with surfactants and thickeners in the same way as suspension concentrates and emulsions, and similar additives are used. This technology allows the controlled release of pesticide active ingredients and can reduce product toxicity appreciably as well as reducing leaching from the soil (Ribeiro *et al.* 2007). Complexity and the high R&D costs tend to deter the smaller agrochemical formulation companies from developing controlled release products. However, recent patents from Syngenta on ''triggered release'' formulations (according to pH, temperature and other factors) suggest that the technology could become very important in future. It could also find applications in seed treatments, where there might be scope for addition of selective herbicides to products, particularly with genetically modified crops. Syngenta, Dow Agro Sciences and Monsanto appear to be in the lead with microencapsulation technology. Syngenta has gained a new lease of life for the insecticide, lambda-cyhalothrin, using its patented ''Zeon technology'' which encapsulates the active ingredient in very small capsules with thin walls. This enables quick ''knock-down'' of insects coupled with long-term persistence. The company has also overcome toxicity problems with the insecticide tefluthrin by producing a capsule suspension as a seed treatment formulation. In a similar way, Monsanto has developed a safer capsule suspension of the maize herbicide acetochlor. Dow is able to encapsulate chlorpyrifos as an emulsion and then convert this into a water dispersible granule by fluid bed spray granulation. Bayer Crop Science has a new technology for coating solid particles with a polyurea/urethane coating. DuPont are looking at liquid wax coating techniques. Further innovations are expected in microencapsulation technology over the next few years which may contribute to safer pesticide use. Significant research is still being expended in the area of microencapsulation technology and there is likely to be further gains from this research. We have developed Lambda Cyhalothrin 10 CS, Lambda Cyhalothrin 25 CS formulations.

Combined/mixed Formulation Technology

Our innovation is the development of a combined (mixed) ZW formulation in the field of agrochemicals for user & environment friendly application of synthetic agrochemicals. It is combination of capsule suspension of lambda cyhalothrin insecticide and concentrated emulsion of chlorpyriphos insecticide. In this unique formulation we have combined two different active ingredients in such a way that one active ingredient i.e. chlorpyriphos will be quickly available/effective just after application on target pests for quick knock-down effect and on the other hand, the other pesticide i.e. lambda cyhalothrin will be efficacious slowly in a controlled manner for long term target pest management. As it is micro encapsulated in a polymer membrane, applicator can apply two pesticides simultaneously in a single application. The product is water based and does not pose the risk of flammability, skin irritation like conventional emsulsifiable concentrate (EC) formulation which contains large amount of organic solvents. The active ingredient lambda cyhalothrin has very good bioefficacy but it causes skin irritation to farmer at the time of application. The micro encapsulation eliminates this problem of skin irritation and itching. Chlorpyriphos is available in market only as EC, its water based EW provides good bioefficacy. The combination will have broad spectrum insecticidal activities and may be used for controlling insects on large number of crops. The technology has been transferred to pesticide industries for commercialization.

Nanotechnology-based Pesticide Formulations

With the development of nanotechnology application in numerous scientific disciplines, it is expected that nanoscale products have been and will be used for agricultural, vector, and urban pest control prior to a complete evaluation of exposure and risk (Kuzma *et al*. 2006). Significant differences may exist between nanotechnology-based pesticides (NBPs) and conventional pesticides, primarily due to size and surface characteristics.

Recent advances in agricultural research have triggered great interest in the exploration of nanotechnology at its nascent stage. Leveraging nanomaterials in plant delivery studies, e.g. carbon nanotubes (CNTs) and metal/ metaloxide nanoparticles (NPs), have been shown to improve seed germination and plant growth (Nair *et al.* 2010). Pesticide nanodelivery techniques, including nanoencapsulates, nanocages and nanocontainers, are more efficient and lead to less pesticide release into the environment and rapid degradation of the pesticide in the soil (Knot *et al*. 2012). The greener nanotechnology approach, with nanoemulsions containing natural oils, surfactants and water, is very promising and could be adopted pragmatically.

Nanogel

Nanogels may be defined as nano-sized hydrogel systems which are highlycross linked systems in nature involving polymer systems, which are either co-polymerised or monomeric (Phillips *et al.* 2010). Sudden outbreak in the field of nanotechnology have introduced the need for developing nanogel systems which proven their potential to deliver active ingredients in controlled, sustained and targetable manner. With the emerging field of polymer sciences it has now become inevitable to prepare smart nano-systems which can prove effective for treatment as well as clinical trials progress (Malmsten *et al*. 2010). Nevertheless, these systems have been investigated from a longer period of time for making advancements in synthetic procedures not only for active delivery but for miscellaneous agents like quantum dots, dyes and other diagnostic agents (Hasegawa *et al*. 2005; Wu *et al*. 2010; Gong *et al*. 2009 & Sun *et al.* 2005)

Traditionally in the name of gels we have heard of semisolid formulations with three dimensional network of organic systems encompassing fluids and drugs. Majorly these systems have been the part of traditional system of topical drug delivery for local effects. Prospects of targeted delivery perhaps could not been established with these preparations (Djordjevic *et al*. 2003). The significance of nano-sized microgel and hydrogel has arisen due to specific delivery system anticipation. Wide variety of polymer systems and the easy alteration of their physico-chemical characteristics have given advantage for versatile form of nanogel formulations (Oishi *et al*. 2007).

Recent studies at clinical level have shown promising value of nanogels (Kageyama *et al*. 2008). Nanogels are typical formulations mainly of the size range of 100 nm, by varying solvent quality and branching the volume fraction, one can alter variably to maintain a three dimensional structure (Mourey *et al*. 2007). The review suggests that innovation in this field shall bring-forth sound support to pesticide applications in future. Recently in our laboratory, we have developed a nanogel formulation of Permethrin (a synthetic Pyrethroid insecticide) for long lasting impregnation of this insecticide in the dresses which can protect personals from mosquito bite whenever they are deployed/posted to work in forest areas. The formulation developed in the laboratory was evaluated as per WHO specifications with respect to wash resistance and it qualifies all the laid down parameters (Patent filling is under process). This type of nanogel formulation may have good future in seed dressing/coating because of its lower particle size, large surface area and greater adhesive properties.

Nanoemulsions

Nanoemulsions have a particle size of less than 200 nm, which makes the systems inherently transparent/translucent and kinetically stable. Pesticides formulated with nanoemulsions having a lower surfactant concentration than microemulsions and surfactants are considerably more environmentally friendly and are cost effective and economically viable (Lim *et. al.* 2011). Low-energy emulsification methods are applied to produce nanoemulsions, and the energy stored could promote smaller-sized nanoparticles of longer life (Lim *et al.* 2011; Sadurni *et al*. 2005; Izquierdo *et al*. 2005). A 5% nanoemulsion formulation of chlorpyriphos was prepared, physic-chemically characterized and larvicidal activity was evaluated against the perpetually troublesome mosquitoes *(Aedes aegypti)* at our laboratory. Efficacy of economically available emulsifiable concentrate was compared with our nanoemulsion by performing larvicidal bioassay on late 3rd and early 4th instar larvae. The experiment was carried out at 26-29°C and relative humidity 65-70%. All treatments were set up in triplicates and percentage mortalities were determined after 24 hours of treatment. Mortality percentage ranged from 88.35-100.00 in nanoemulsion and 86.67-98.35 in EC, respectively (Table 2). It can be predicted that at lower concentration (300-1500ppm), nanoemulsion can be very effective against mosquitoes due to smaller droplet size

Table 2.
Percentage mortality of *Aedes aegypti*

Serial No.	Conc. (ppm)	% mortality after 24 hrs (EC)	% mortality after 24 hrs (Nanoemulsion)
1.	300	86.67	88.35
2.	600	93.13	93.35
3.	900	95.35	96.65
4.	1200	96.65	98.35
5.	1500	98.35	100.00
6.	Control	0.00	0.00

of nanopesticide with increased surface area and better surface coverage property.

Conclusion

With the many pressures on product performance, formulation is becoming a key technology by which agrochemical companies can differentiate their products and add significant value. New product introduction is an important factor in brand refreshment and new formulation technology can impact this considerably. This article has described some of the changes occurring in formulation types employed and the further trends that are driving technologies such as examples of water-based dispersion formulation technology for oil-in-water emulsions, suspensions, microemulsions etc. as well as other formulation types such as gel and dry product formulations where new techniques of formulation, often combining polymers and surfactants in novel ways have resulted in a relatively safe and environment friendly product. Moving with a lustrous record of providing quality products to its customers since past many years, IPFT''s scientists is now shifting its focus towards 'Nanotechnology', keeping in view the hazardous effects of chemical pesticides. Since Nanotechnology has been described as a "Sunrise sector" by industries, IPFT is now on its adventurous journey towards exploring potentials of Nanotechnology in the field of pesticides.

Literature Cited

Beestman GB. 2003 Controlled release in crop protection: past experience and future potential, pp. 272-279. In *Chemistry of crop protection, progress and prospects in science and regulation* (Eds Voss G Ramos G) Wiley-VCH Verlag GmbH & Co, Weinheim.

Djordjevic J Michniak B Uhrich Kathryn E. 2003 Amphiphilic star like macromolecules as novel carriers for topical delivery of non steroidal anti-inflammatory drugs. *AAPS PharmSciTech* **5**(4): 1-12.

Fernández-Pérez M. 2007 Controlled release systems to prevent the agro-environmental pollution derived from pesticide use. *Journal of Environmental Science and Health B* **42**:857-62.

Geisler G Hellweg S Liechti S Hungerbüler K. 2004 Variability assessment of groundwater exposure to pesticides and its consideration in life-cycle assessment. *Environmental Science and Technology* **38**:4457-64.

Gong Y Fan M Gao F Hong J Liu S Luo S Yu J Huang J. 2009 Preparation and characterization of amino functionalized magnetic nanogels via photopolymerisation for MRI applications. *Colloids and Surfaces B* **71**:383-407.

Green JM Beestman GB. 2007 Recently patented and commercialized formulation and adjuvant technology. *Crop Protection* **26**: 320-27.

Gupta PK. 2004 Pesticide Exposure-Indian Scene. *Toxicology* **198**:83-90.

Harper S Usenko C Hutchison J Maddux B Tanguay R. 2008 Proactively designing nanomaterials to enhance performance and minimize hazard. *International Journal of Nanotechnology* **5**:124-42.

Hasegawa U Nomura ICM Kaul SC Hirano T Akiyoshi K. 2005 Nanogel quantum dots hybrid nanoparticles for live cell imaging. *Biochemical and Biophysical Research Communications* **331**:917-21.

Hewin International. 2000 Surfactants and other additives in Agricultural Formulations, Published by John Wiley and Sons Inc., New York, USA.

Hiromoto B. 2007 Pesticide microemulsions and dispersant/penetrant formulations. *United States Pat-*

ent, Patent No: US 7297351.

Izquierdo P Feng J Esquena J Tadros ThF Dederen JC Garcia MJ. 2005 The influence of surfactant mixing ratio on nanoemulsion formation and stability. *Journal of Colloid and Interface Science* **285**:388-94.

Kageyama S Kitano S Hirayama M Nagata Y Imai H Shiraishi T. 2008 Humoral immune responses in patients vaccinated with 1-146 HER-2 protein complexed with cholesteryl pullulan nanogel. *Cancer Science* **99**(3):601-07.

Knowles A. 2008 Recent developments of safer formulations of agrochemicals. *Environmentalist* **28** (1): 35-44.

Kuzma J VerHage P. 2010 Nanotechnology in agriculture and food production: Anticipated applications. www.document] URLhttp:// www.nanotechproject.org/file_download/ files/ PEN4_AgFood.pdf.

Lim CJ Basri M Omar D Rahman MBA Salleh AB and Rahman RNZRA. 2011 Self-assembly behaviour of alkylpolyglucosides (APG) in mixed surfactant-stabilized emulsions system. *Journal of Molecular Liquids* **158**:175–181.

Malmsten M Bysell H Hansson P. 2010 Biomacromolecules in macrogels – Opportunities and challenges for drug delivery. Curr. Opin. *Colloid & Interface Science* **1**:6-18.

Mathur SC. (1999) Future of Indian pesticide industry in next millennium. *Pesticide Information* **24**(4): 9.

Mourey TH Leon JW Bennet JR Bryan TG Slater LA Balke ST. 2007 Characterizing property distributions of polymeric nanogels by size-exclusion chromatography. *Journal of Chromatography A.* **11(**46): 51-60.

Mulqueen P. 2003 Recent advances in agrochemical formulation. *Advances in Colloid and Interface Science***106**: 83-107.

Nair R Varghese SH Nair BG Maekawa T Yoshida Y Kumar DS. 2010 Nanoparticulate material delivery to plants. *Plant Science***179**:154-63.

Oishi M Miyagawa N Sakaru T Nagasaki Y. 2007 pH-responsive nanogel containing platinum nanoparticles: Applications to on-off regulation of catalytic activity for reactive oxygen species. *Reactive Functional Polym*ers **67**:662-68.

Phillips MA Gran ML Peppas NA. 2010 Targeted nanodelivery of drugs and diagnostics. *Nano Today* **5**:143-59.

Sadurni N Solans C Azemar N Garcia-Celma MJ . 2005 Studies on the formation of O/W nano-emulsions, by low-energy emulsification methods, suitable for pharmaceutical application. *European Journal Pharmaceutical Science* **26**:438-451.

Sun H Yu J Gong P Xu D Zhang C Yao S 2005 Novel core shell magnetic nanogels synthesized in an emulsion free aqueous systems under UV irradiation for targeted radiopharmaceutical applications. *Journal of Magnetism and. Magnetic Materials* **294**:273-80.

Tadros TF. 1995 Surfactants in Agrochemicals, Marcel Dekker, New York, USA.

Wu W Aiello M Zhou T Bernila A Banerjee P Zhou S. 2010 In situ immobilization of quantum dots in polysaccharide based nanogel for integration of optical pH sensing, tumor cell sensing and drug delivery. *Biomaterials* **31**:3023-31.

Zabkiewicz JA. 2000 Adjuvants and herbicidal efficacy –present status and future prospects. *Weed Research* **40**: 139-14.