Research Dissertation

FOR

INVESTIGATING THE EFFECT OF VARIOUS FILM-FORMING POLYMERS ON THE EVAPORATION RATE OF A VOLATILE COMPONENT IN A COSMETIC FORMULATION

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I declare that this is my own work and that this dissertation, nor any part thereof, has previously been submitted to another university.

Carla Barnard

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EXECUTIVE SUMMARY

The topical application of many substances, including drugs, enzymes, moisturizers and fragrances, contributes largely to the cosmetic and pharmaceutical industries. These components are often volatile in nature and dissipate in a matter of hours. When considering the different types of slow release systems, an overwhelming variety of these systems is available. Each one of the systems is unique in a way, and is designed to perform a particular function, whether it facilitates the controlled release of an active into the body via the skin surface (transdermal delivery) or whether it reduces the rate of loss of an active from the skin surface to the surrounding environment.

For the purpose of this study, a previously existing fixative formulation which is believed to reduce the rate of loss of an active component to the environment, through film formation on the skin surface, was investigated. Alternative ingredients or components were incorporated together with the original fixative formulation ingredients into an experimental design which investigates the effect of each group of the components present. 18 formulations with various concentrations of the components within the groups and specified upper and lower limits for each component were formulated. The fixative properties of the formulations were analysed through the incorporation of a fixed amount of a simple fragrance molecule, 4-methoxybenzaldehyde, into each formulation and evaporation studies were conducted in an environmental room at 28±1° C over a period of 5 hours followed by gas chromatography analysis and finally data analyses using statistical methods. .

The most efficient fixative formulation was established using regression analysis. The fragrance compound in this formulation was found to evaporate at a rate of 0.47 g/L per hour. The least efficient fixative formulation lead to the loss of 0.78 g/L of the fragrance component per hour.

From the calculated fragrance concentrations, the rate constant for each individual fixative formulation could be calculated and response surface

modelling by backward regression was used in order to determine how each component contributes to the rate of loss of the fragrance compound. Since the sum of the original ingredient and its alternative was constant, each of the original ingredients was coupled directly to its alternative and no conclusion could be made about the contribution of individual components. By increasing the concentration of Hydroxypropylcellulose (HPC) 100K and its alternative HPC 140K, while keeping the effects of the other components constant, a decrease in the rate of fragrance loss was observed. The same conclusion could be made when increasing the concentrations of PEG-12 Dimethicone and its alternative cetyl dimethicone (decreases the evaporation rate). An interaction took place between HPC 100K and PEG-12 dimethicone and their alternatives. The negative effect was, however, not as strong as the combined positive effect on the rate of fragrance loss of the individual components HPC and PEG-12 dimethicone. Evidence suggested that the removal of the components polyvinylpyrrolidone and its alternative, polyurethane-32 (Baycusan® C1003), would improve the effectiveness of the fixative formulation in terms of its slow release properties. A confirmation experiment established that the exclusion of these components from the fixative formulation does improve the “slow release” properties thereof.

A larger, more intricate design is required to investigate the effect of each one of the individual components and where the sum of the components (original and its alternative) is not constant.

Key words:
Fixative, formulations, slow release, rate constant, evaporation rate.

CHAPTER 1

BACKGROUND STUDY

The topical application of substances such as drugs, enzymes, moisturizers, fragrances as well as a whole range of other cosmetic and pharmacological molecules has historically been utilized by humans for many centuries[1]. Often, scents and odours giving fragrances their unique qualities are short lived and dissipate within a matter of hours. This holds true especially in the case of aerosol sprays used for colognes, perfumes and other cosmetic applications to either hair or skin. Due to the high pressure and high rate of evaporation of the driving power, many of the top notes of the desired scent dissipate rapidly and the end note emerges in the absence of the top and middle components[2]. For this reason, the slow release of perfumes and perfumes incorporated into various cosmetic products is very important[3]. Therefore the use of an appropriate vehicle or carrier for the delivery of the active to the skin (topical application) is of critical importance.

1.1 Background to project

Upon consideration of the above, I proposed to formulate a slow-releasing perfume cream for my B Sc Honours project in 2009. The aim of the project was to select an appropriate slow release system with the ultimate goal of producing a slow-releasing perfume cream facilitating the sustained release of the incorporated active over a period of time exceeding six hours. A fixative formulation (derived from US Patent 6,172,037 and using it as a broad guideline[4]) was incorporated into a formulation containing an active component (4-methoxybenzaldehyde) and aqueous cream. The fixative formulation remained unchanged in terms of its composition. These three components were varied in concentration in order to determine whether the inclusion of a fixative component does in fact reduce the rate of evaporation of the active component. The most efficient combination of these three components in terms of the slow release properties of the mixture (active,

aqueous cream and fixative component) was also determined, but this was however simply a pilot study and could only be used as a guideline for the purposes of this study. In the most efficient mixture from 2009, 6 % w/w of the fixative formulation, and 2 % w/w of the active component was included in the formulation (92 % aqueous cream). The method used to determine the evaporation rate of the active differed from the method used for this study, and therefore the results from the 2009 study could not be compared directly to the results from this study.

The objectives for the proposed slow release perfume cream (2009) were as follows:

1. Controlled release of fragrance from skin surface.
2. Elegant feel – not greasy or tacky.
3. Moisturising properties.
4. Easy to apply to skin – good spreadability.
5. Non-irritating, non-toxic product suitable for topical application.
6. Avoidance of the use of volatile organic compounds where possible (an environmentally friendly product).

While the concept of a perfume cream was demonstrated successfully during this project, the ability of the slow release formulation (perfume carrier) to retain the perfume active was limited. In the light of these prior results, it was therefore decided to undertake a study aimed at investigating the development of a more effective slow release or fragrance fixative.

1.2. Literature study

A large proportion of the research was aimed at the identification of possible alternatives for the ingredients in the original formulation (from 2009), and therefore many material safety data sheets and chemical company information brochures for specific ingredients are cited as references.

Novel controlled-release systems for consumer applications should fulfil the following requirements[5].

1. Release over a period of 6-12 hours;
2. Controlled (constant) release;
3. Use of non-toxic and non-carcinogenic polymers; and
4. Use of polymeric systems relatively stable to prolonged storage periods.

There are five major slow release systems previously investigated by other researchers. These are the following:

1. Encapsulation (Liposomes[6,7,8] and microcapsules[9]);
2. Emulsions (w/o and o/w[10,7]);
3. Multiple-, micro- and nano-emulsions[11];
4. Chemical or complex formation[12,13];
5. Polymers[14,9,5].

These alternatives were investigated for the 2009 perfume cream project. Encapsulation and emulsions are used primarily for trans-dermal treatment which is inappropriate for this study, and emulsions are often too unstable. Chemical methods are not desirable since they are often complicated. Polymers are very stable, decrease the evaporation rate and facilitate the slow release of the entrapped fragrance molecules to the environment. Polymers are also biocompatible and easy to obtain in various forms such as beads or microbeads, films (trans-dermal stamps) or compressed[15]. For these reasons the use of polymers, as the most appropriate slow release system, was preferred above encapsulation, emulsions and chemical methods.

As can be expected, polymers play a crucial role in film formation. An active ingredient (e.g. a fragrance) can be formulated with a polymer to form a thin film over the skin surface. Examples of where such systems have been used commercially include insect repellents such as Sawyer Controlled Release®, HourGuard® and Ultrathon®. The most commonly used polymers facilitating the slow release of perfumes include poly(ethylene glycol), hydroxylated

poly(meth)acrylates, ethylene-vinyl acetate copolymers and polyolefins. Some natural polymers frequently used include chitosan, alginate or cellulose – these being non-toxic, less expensive and highly abundant in nature[5,9].

Polymers also perform a wide array of functions in, for example, cosmetic applications, making them a useful addition to various formulations. They function as pigment dispersants, skin conditioners, lubricants, water-proofing agents (e.g. sunscreens), rheology modifiers in gels and lotions and emulsifiers[14]. The film formed by polymers also prevents trans-dermal water loss. Other advantages include enhanced rub off and water resistance of cosmetic products as well as increased fragrance longevity through the entrapment of the active resulting in an observed decrease in its evaporation rate[15]. One of the other major benefits of incorporating these functional polymers into formulations is that they reduce irritancy and greasiness associated with low molecular weight raw materials, whilst delivering the same characteristic properties.

The polymers to be investigated for the purpose of this study include:

1. Hydroxypropylcellulose
2. SF1288 (PEG-12 Dimethicone)
3. Polyvinylpyrrolidone-K30
4. JR-30 (polyquaternium-10)

Alternatives to these polymers will also be investigated in order to study their potential effects on the rate of fragrance loss.

1.3 Polymer properties and alternatives

Film formers can be divided into the following five classes[16]:

1. Acrylates
2. Polyurethane-acrylates
3. Polyvinylpyrrolidones
4. Cellulose derivates

5. Silicones

Polymers in these classes produce films which have the following favourable properties[16]:

1. Low viscosity
2. Drying time less than 5 minutes
3. Low outward stickiness
4. High cosmetic attractiveness
5. Integrity of film on skin after 18 hours: complete film, no cracks or flaking.

Since these characteristics are crucial in the selection of appropriate film-forming alternatives for use on human skin, some of the above mentioned film-formers will be investigated in greater detail during this study as part of the fragrance fixative formulations.

The following ingredients are present in the original fragrance fixative formulation (Refer to Appendix A for the formulation):

1. Polyvinylpyrrolidone (PVP-K30)
2. PEG-12 Dimethicone (SF1288)
3. Propylene Glycol
4. Hydroxypropylcellulose
5. Coconut oil (CDE)
6. Polyquaterium-10 and distilled water (JR30/water)

Each one of these constituents will be discussed in detail with respect to its main function within the formulation. The most viable alternatives will then be discussed and selected for the purposes of this study.

1.3.1 Polyvinylpyrrolidone (PVP)

Safety

Polyvinylpyrrolidone is the linear polymer of 1-vinyl-2-pyrrolidone monomers[8]. Based on the data available (short term PVP inhalation, animal studies, tests conducted to test for sensitization of skin, oral tests etc.) PVP is safe to be used in cosmetic applications[17].

Applications

PVP has a wide array of functions and applications in many industries including pharmaceuticals, cosmetic products and paints. It is frequently used as a binder, emulsion stabiliser, film former, hair fixative, and suspending agent-nonsurfactant[17]. It is also widely used due to its excellent hygroscopic properties, complexing ability and physiological compatibility[18]. In the field of cosmetics in particular, PVP is used as a filming-agent, viscosity–enhancement agent, lubricator and adhesive, forming key components in hair sprays, mousse gels and lotions, shampoos, lip-sticks, sunscreens, and lotions in skin care products, eye make-up and deodorants[18].

Problems/issues

One of the major problems associated with PVP is the formation of a film which is often perceived as being tacky. The properties associated with this kind of film former are also difficult to control, often resulting in the formation of a brittle film[19].

Alternatives

Alternatives considered for PVP-K30 include the following:

1. Poly(vinyl acetate) (PVAc)
2. Poly(vinyl alcohol) (PVA)
3. Poly(vinylpyrrolidone-co-vinyl acetate) (PVP/VA copolymer)
4. PVP/Acrylate copolymer
5. Polyurethane-32 (Baycusan® C 1003)
6. Polyurethane-14 (and) AMP-Acrylates Copolymer

Tables 1 and 2 summarize the properties and uses of the above-mentioned filming forming agents.

Table 1: Applications of various PVP alternatives.

	Film former	Hair fixative resin	Thickener	Dispersant	Lubricant	Skin protectant	Emulsion stabiliser	Binder
[20,21]PVP	✓	✓	✓	✓	✓	✓	✓	✓
[22]Polvinyl acetate	✓							
[23]Polyvinyl alcohol	✓	✓ (of oil portion)		✓ Emulsifying and adhesive	✓	✓	✓	✓
[20]PVP/VA copolymer	✓	✓						
[20]PVP/Acrylates copolymer	✓	✓						
[24]Polyurethane-32 (Baycusan® C 1003)	✓ (also plasticizing effect)				✓			
[25] Polyurethane-14 (and) AMP-Acrylates Copolymer (DynamX®)	✓				✓			

Table 2: Characteristics of polyvinylpyrrolidone and selected alternatives.

	Form (solid/liquid)	Compatibility & formulations considerations	Safety (CIR Expert Panel)	Suggested use
[20,21]PVP	Powders and aqueous solutions	Insoluble in hydrocarbons. Water soluble.	✓	1<1% in skin care products.
[22]Polyvinyl acetate (hard and brittle film according to ChemQuest Group Inc.)	Solid beads, clear	Water insoluble, slightly hydrophilic. Insoluble in oils, fats and gasoline. Ester groups present renders it reactive with alkalis.	✓	
[22,26,23] Polyvinyl alcohol	White or light yellow. In form of floccules, flakes or solid powder.	Soluble in water, slightly soluble in ethanol and insoluble in other organic solvents.	✓	
[20]PVA/VA copolymer	PVA/VA S-630 supplied as a white powder, all others supplied as alcoholic solutions, in which the solvent is either ethanol or isopropanol or water.	Soluble in ethanol and isopropanol. Formulation considerations depend on grade: high vinyl acetate content – relative insoluble in water. All are soluble in ethanol. Insoluble in hydrocarbaon alone. Compatible with wide range of hairspray ingredients.	✓	2-6% in gel setting lotions; 4-8% in hair fixatives, 2% in coatings.
[20]PVP/acrylate copolymer	Alcoholic solutions.	Alcohol and alkaline solutions. Formulation considerations: neutralized, neutralize 20-100% for best results (necessary for water solubility).		5-85% in hair fixative formulations.
[24,27] Polyurethane-32 (Baycusan® C1003)	Low viscosity, white liquid.	Compatible with wide range of cosmetic ingredients including synthetic and natural thickeners. Limited compatibility with cationic ingredients.	✓ Not classified as a hazardous product	At least 40% wt. % to form a continuous film on skin.
[25] Polyurethane-14 (and) AMP-acrylates copolymer (DynamX®)	Amber liquid. 10 Supplied as 28% solution in ethanol (25%) / water (47%).	Water soluble.	Not safe. May cause de-fatting of skin resulting in dryness or dermatitis upon repeated exposure.	

From Tables 1 and 2, the most suitable alternative was identified as Polyurethane-32 (Baycusan® C 1003). It was selected since the film properties of this particular polyurethane are similar to that of PVP, which should result in a similar role, if any, in the controlled release of active substances.

Even though polyvinyl alcohol seems to be the most promising alternative, polyurethane-32 (Baycusan® C1003) has been suggested as a suitable alternative to polyvinyl alcohol (especially in cosmetic formulations such as peel off masks). Attributes of this particular polyurethane include film formation purely through physical drying, facilitated by the evaporation of water through coalescence of the particles dispersed therein. A natural plasticizing effect is also obtained through the small amount of non-evaporated water which facilitates in the formation of a continuous, homogeneous film with minimal inclusion of polyurethane-32[28]. This makes it an extremely cost-effective alternative. Glycerine and anionic polymers (e.g. xantham gum) may also be used in combination with polyurethane-32 to facilitate in the manipulation of the mechanical properties of the film formed (plasticizing effect) [28]. An article by Viala et al. (2008)[29] also suggests that polyurethane-32 (Baycusan® C1003) can be used as an alternative to PVA, predominantly due to the fact that it produces a highly flexible film[27].

1.3.2. SF1288: PEG-12 Dimethicone

Safety

PEG-12 dimethicone, is a term used to describe a group of polymers which are synthesised from dimethicone and polyoxyethylene and/or polyoxypropylene[30]. It is soluble in alcohol, water and hydro-alcoholic systems[31]. According to an assessment by the Cosmetic Ingredient Review (CIR) Expert Panel, it was scientifically proven that dimethicone copolyols are safe to use in cosmetic products.

Applications

Silicones are often included in formulations due to their film forming properties, providing substantivity, wash-off resistance and protection. It has been experimentally proven that the incorporation of silicones into formulations produces the sustained, longer-lasting release of fragrances relative to a control where no silicones were present (4 hours longer than control)[32].

Silicones which are used in the cosmetic industry are grouped into categories which include: cyclic, linear, or organo-functional polydimethylsiloxanes (PMDS), as well as silicone elastomer dispersions and resins. These silicones contribute to attributes such as good spreading ability, film forming, wash-off resistance, skin feel, volatility, and permeability[33].

In the cosmetic industry, some of the main uses of dimethicone copolyols are in the formulation of hairsprays, wave sets, hair conditioners, shampoos, shaving products and some make-up and skin care products – the main functions being the conditioning of both hair and skin. They act as surface tension depressants, conditioners, detackifying greasy formulations, are good foam builders and require low usage levels[31]. Silicones also contribute towards emollient properties of formulations; act as water barriers and as emulsifiers. In relation to sensory characteristics, they are smooth and silky with a non-greasy feel. This is attributed to the fact that they have low coefficients of friction, are liquids at high molecular weight, and have low surface tensions – all together producing a positive skin feel[33].

Problems/Issues

Since silicones have many different properties, careful considerations should be made when formulating, especially in terms of their solubility.

Alternatives

Alternatives considered for SF1288 (PEG-12 Dimethicone) include the following:

1. Elastomers
    - Cyclopentasiloxane (and) Dimethicone Crosspolymer (BC 2471 Silicone Elastomer Blend).
    - Isododecane (and) vinyldimethyl/trimethyl siloxysilicate dimethicone crosspolymer (Wacker-Belsil® RG90).
    - Cyclopentasiloxane, Dimethicone/vinyltrimethylsiloxysilicate crosspolymer (Wacker-Belsil® RG100).
    - Dimethicone/Vinyl Dimethicone Crosspolymer (and) silica (Dow Corning 9701 Cosmetic Powder).
2. Blends
    - Dimethiconol and Dimethicone (Dow Corning® Dimethiconol Blend 20).
    - Cyclopentasiloxane (and) Dimethicone Crosspolymer (Dow Corning® ST-Elastomer).
3. Waxes
    - Stearoxytrimethyl silane and stearyl alcohol (Dow Corning® Silky Wax 10).
4. Cetyl dimethicone (Dow Corning® 2502 Cosmetic fluid).

Tables 3 and 4 summarize the applications and properties of the above compounds.

Table 3: Applications of various PEG-12 Dimethicone alternatives.

	Emollient	Lubricant	Film former	Silky soft feel	Additional
[34,35]PEG-12 Dimethicone	✓	✓	✓ (hydrophobic)	[1] ✓	Detackifies greasy formulations, wetting agent, emulsifier, foam builder, surface tension depressant.
[36] Isododecane (and) vinyldimethyl/trimethyl siloxyslilicate stearyl dimethicone crosspolymer			✓ (hydrophobic)	✓	
[37,38]Cyclopentasiloxane, Dimethycone/vinyltrimethyl-siloxysilicate crosspolymer		✓	✓ (hydrophobic)	✓	
[39,40] Dimethicone/Vinyl Dimethicone Crosspolymer (and) silica				✓	
[40]Cyclopentasiloxane (and) Dimethicone Crosspolymer	Improves spreadability				Enhances gloss
[42,43]BLEND Dimethiconol and Dimethicone		✓ Improves spreadability		✓	Substantive on skin, non-occlusive, water repellent.
[44,45]BLEND Cyclopentasiloxane (and) Dimethicone Crosspolmer				✓	Quick absorption, reduces tack, thickening agent for w/o and w/s formulations, cyclomethicones and other silicone fluids.
[46,47]WAXES Stearoxytrimethyl silane and stearyl alcohol	✓	✓	✓	✓	Semi-occlusive, detackifier, thickening agent, water repellent, compatible with organic ingredients.
[48]Cetyl dimethicone				Controlled moisturization	Substantive to skin, enhances SPF of organic and inorganic sunscreens, improves shine, non-acnegenic, non-comedogenic.

Table 4: Characteristics of PEG-12 Dimethicone and selected alternatives.

	Form (solid/liquid)	Compatibility & formulation considerations	Safety (CIR Expert Panel)	Suggested use
[34]PEG-12 Dimethicone	Amber liquid.	Soluble in alcohol, water and hydro-alcoholic systems.	✓	0.1-2.0 % in skin creams to improve emolliency and lubricity of formulations.
[41]ELASTOMER Cyclopentasiloxane (and) Dimethicone Crosspolymer	Clear, soft gel.	Not soluble in water. Could be added into: oil or silicone phase of an emulsion; post-added to viscous creams; pre-dispersed in cyclomethicone or dimethicone before addition to a formulation.	✓	0.01-30%, preferable 1-10%.
ELASTOMER [49,36]Isododecane (and) vinyldimethyl/trimethyl siloxyslilicate stearyl dimethicone crosspolymer	Colourless, translucent gel.	Formulated in: o/w, w/o, or w/si-emulsions. Also in anhydrous systems, but preferred method is to disperse it in the suitable oils or solvents. Soluble in certain ester oils, silicone oils, triglycerides, alcohol and water. Insoluble in water.	✓	
ELASTOMER [37,39]Cyclopentasiloxane, Dimethycone/vinyltrimethyl-siloxysilicate crosspolymer	Clear, colourless gel.	Soluble in some ester oils (Isopropyl Myristate, dicaprylyl Ether) and some silicone fluids (Wacker Belsil® DM 0.65, DM1 plus, PDM 20, 200, 1000).	✓	
ELASTOMER [39,40]Dimethicone/Vinyl Dimethicone Crosspolymer (and) silica	White silicone powder with silica coating.	Can be added directly to oil phase ingredients without doing a premix in another fluid.	No significant irritation observed upon single or short term application, but may cause slight skin irritation upon prolonged or repeated application.	Threshold values are as follows: water-in-silicone emulsion: 4%; hydrogel formulations: 3%; for silicone-in-water emulsion: 3% when using an organic co-emulsifier and 2% when using silicone co-emulsifier.
BLEND [42,43]Dimethiconol and Dimethicone	Colourless odourless liquid.	Miscible with silicones, isopropyl myristate, mineral oil, non-ionic surfactant (sorbitan monooleate). Non-soluble in water. Recommended: when making an emulsion – use high speed and pass through homogenizer.	Irritation not expected from a single or from short-term exposure.	

Table 4: Continued.

	Form (solid/liquid)	Compatibility & formulation considerations	Safety (CIR Expert Panel)	Suggested use
BLEND [44,45]Cyclopentasiloxane (and) Dimethicone Crosspolmer	Light straw, odourless, thixotropic solid. 43Crystal clear to slightly translcucent gel. May also observe slight yellow to brown colour.	Compatible with: fatty esters such as isopropyl myristate and octyl palmitate; hydrocarbons such as mineral oil (10% w/w) and silicones such as Corning ST-cyclomethicone 5-NF. May be added to oil or silicone phase in an emulsion formulation (w/o, o/w, w/s); or post added to emulsions if the emulsion is viscous enough. Can decrease viscosity by blending with dimethicone or cyclomethicone.	No significant irritation is expected from short term or a single exposure.	BLEND [43,44]Cyclopentasiloxane (and) Dimethicone Crosspolmer (Dow Corning® ST-Elastomer).
WAXES [46,47]Stearoxytrimethyl silane and stearyl alcohol	At room termperature: soft white to light straw, semi-crystalline. At 60° C: clear liquid with no precipitate.	Soluble in wide range of materials, including: Alcohol (ethanol 95% and isopropanol 99%), propylene glycol (at 70° C). Not miscible in water, vegetable oil (at 70 °C), glycerol and glycerine.	No significant irritation is expected from short term or a single exposure.	WAXES [45,46]Stearoxytrimethyl silane and stearyl alcohol (Dow Corning® Silky Wax 10).
[48]Cetyl DImethicone	Colourless to pale yellow liquid.	Oil soluble. Heat liquid to 40° C before adding to the oil phase to ensure homogeity.	No adverse effects expected when inhaled, ingested or in case of skin contact. Temporary discomfort upon eye contact.	Suggested levels 1-5 % w/w in personal care formulations.

From Tables 3 and 4, it was concluded that cetyl dimethicone would be the most suitable alternative to PEG-12 Dimethicone. Cetyl dimethicone basically consists of a linear polysiloxane surrounded by randomly distributed alkyl chains. This cosmetic fluid was developed specifically for use in skin and hair care as well as colour cosmetic applications. It is compatible with a wide variety of organic cosmetic ingredients.

PEG-12 Dimethicone is representative of the group know as Polydimethylsiloxanes (PDMS), which are straight chain, linear silicones. While PEG-12 Dimethicone is incorporated into the water phase of the original formulation, cetyl dimethicone (DC 2502 Cosmetic fluid) has to be incorporated into the oil phase of the formulation. Homogeity is ensured by heating the chemical to 40˚ C prior to addition to the formulation.

1.3.3 Propylene Glycol (PG)

Safety

Propylene glycol is a petrolatum derivative, also known as propane-1,2-diol. It is a synthetic, clear, colourless, hygroscopic, viscous liquid soluble in water, alcohol and acetone[50]. This ingredient is however linked to sensitivity reactions which include local irritation, allergic reactions, autoxicity, kidney damage, and liver abnormalities. It is toxic to human cells in culture, an irritant and sensitizer causing dryness, erythma (abnormal redness) and blistering. Despite this data, PG is still generally regarded as safe and is one of the most frequently used ingredients in cosmetic products[51].

Applications

Propylene glycol is a humectant, primarily functioning as a moisturiser. In conditions where the humidity exceeds 80%, humectants are able to attract water from both the surrounding atmosphere and underlying skin layers towards the surface layers of the skin. The danger lies in low humidity conditions however, where trans-epidermal water loss (TEWL) from the dermis and epidermis takes place resulting in conditions such as xerosis.

This problem is addressed by including an occlusive (Section 2.3.5) together with the humectant in formulations[52].

Propylene glycol is extremely versatile and used in, for example, the cosmetic industry in the manufacture of spray deodorants, baby lotions, emollients/moisturisers, lipsticks and suntan lotions. It also facilitates in the decreased dehydration rate of cosmetic creams[53].

Alternatives

Upon investigation of possible alternatives to propylene glycol for the original formulation, a common trend in recommended humectants was observed. The following statements were made and are cited from various sources:

1. The use of sorbitol, glycerine or gelatine has been suggested repeatedly[54].
2. Glycerol, sorbitol and lecithin are good humectants[55].
3. Glycerine and sorbitol are good moisture retention agents[56].

When considering these recommendations, the following alternatives to propylene glycol, for the purpose of this study, were considered:

- Glycerine
- Gelatine
- Sorbitol
- Lecithin

Tables 5 and 6 summarize the applications and properties of the above compounds.

Table 5: Applications of Propylene Glycol and selected alternatives.

	Humectant	Emollient	Binder	Film former	Additional
[50]PG	✓				Solvent
[51]Glycerine	✓	✓			Plasticizer, thickener, solvent, dispersing medium, lubricant
[20]Cosmetic Gelatine	✓			✓	emulsion stabiliser, thickening agent, skin protectant, anti-irritant
[20]Gelatine			✓		protein conditioner
[64]Sorbitol	✓				
[47]Lecithin	✓	✓	✓	✓	Emulsifier, dispersant, moisturizing, Skin feel, refatting agent, restructuring, hydrating, soothing, wetting agent, adhesion improver, stabilizer, fat crystallization inhibitor, hair gloss, thickening agent, liposome-former, encapsulation

Table 6: Characteristics of propylene and selected alternative.

	Form (liquid/solid)	Compatibility & formulation considerations	Safety (CIR Expert Panel)	Suggested use
[50,57,58]Propylene glycol	Clear, colourless, hygroscopic, viscous liquid.	Soluble in water, ethanol and acetone.	Unsafe	Propylene glycol can be used safely in cosmetics up to concentrations of 50%.
[51,59]Glycerine	Clear, colourless liquid.	Miscible in cold water, hot water and alcohol. Partially soluble in acetone. Slightly soluble in diethyl ether. Limited solubility in ethyl acetate. Insoluble in carbon tetrachloride, benzene, chloroform, petroleum ethers, and oils.	✓	
[20]Cosmetic gelatine	Crystalline powder.	Add to water, heat to 80°C to dissolve – thickens as it cools.	Regulatory status: cosmetic	2% in moisturizers as a humectant, skin protectant, 1% in emulsions to thicken and stabilize.
[20]Gelatine	Buff crystalline powder.	Water soluble. Dissolve in water before addition. Do not heat above 40°C (soluble in most polar solvents).	Regulatory status: NF grade.	1-5% in skin creams and lotions.
[60,61,62]Sorbitol	White, odourless, sweet tasting powder.	Solubility in water, g/100 ml at 20°C : 220.	✓	
[63]Lecithin	Waxy mass to a thick pourable liquid.		Safe to use in rinse-off products. Leave on products: concentration limited to ≤15%.	≤15% (1).

Since propylene glycol functions as the solvent for hydroxypropylcellulose and in addition to PVP and coconut oil, makes up phase B (oil phase) of the final formulation, it was decided that propylene glycol would not be replaced by an alternative. Upon in depth investigation of alternative ingredients, it became clear how common the use of propylene glycol is in various cosmetic formulations. The suggested upper usage level of propylene glycol is 50% within a formulation. This upper limit was exceeded (68 %) in the original (2009) formulation since the fixative formulation in itself is never used as is, but always as a component within a formulation which means that the percentage of this particular component present in a final formulation will never exceed the suggested 50 % upper limit.

1.3.4. Hydroxypropylcellulose (HPC)

Safety

Hydroxypropylcellulose is a derivative of cellulose (ether) and is soluble in both water and organic solvents. It is a free flowing, granular powder which can be dispersed in water at 60° C[20]. It is a highly flexible polymer which has the ability to form a film characterised by high elongation and moderate tensile strength. It also displays thermoplastic behaviour and when manufactured with high hydroxypropyl substitution it requires little or no plasticizer[66]. According to the Cosmetic Ingredient Review (CIR) Expert Panel, HPC is safe to use[67].

Applications

HPC functions as a thickener, foam stabilizer, rheology modifier and film former[12].

Alternatives

The alternatives considered for HPC include the following:

- Carboxymethylcellulose (CMC)
- Methylcellulose (MC)
- Hydroxypropylmethylcellulose (HPMC)
- Hydroxyethylcellulose (HEC)
- Different Viscosities of HPC
    - J CS: Molecular weight 140,000
    - G CS: Molecular weight 370,000
    - M CS: Molecular weight 850,000

Tables 7 and 8 summarize the properties and uses of the above-mentioned filming forming agents.

Table 7: Applications of HPC and selected alternatives[20].

	Film Former	Emulsion/foam stabiliser	Viscosity incr. agent/thickener	Binder	Rheology modifier
HPC	✓	✓	✓	✓	✓
CMC	✓	✓	✓	✓	✓
MC		✓	✓	✓	
HPMC	✓	✓	✓	✓	
HEC	✓	✓	✓	✓	✓
M CS	✓		✓		
G CS	✓		✓		
J CS	✓		✓		

Table 8: Characteristics of hydroxypropylcellulose and selected alternatives[20].

	Form (s/l)	Compatibility and formulation considerations	Safety (CIR Expert Panel)	Suggested use
*HPC	Free flowing powder, granular powder. (Disperse in water @ 60° C and cool to hydrate).	Good in water (<45° C) and polar organic solvents (EtOH).	✓	<1% in shaving creams; <1% in hair styling products
CMC		Water soluble	✓	
MC	Granulated or in powder.	Soluble in water	✓	1-2% in linaments; 1-2% in toothpaste; 1-2% in creams.
HPMC	Powder, granulated	Cold-water soluble (some grades of methocel are efficient, good clarity thickeners that are surface treated to enable direct addition to tap water of pH≤7.5.	✓	0.5-0.8% in shampoo, 0.8% in cleansing gels, 0.5% in hair conditioners, 0.4% in cosmetic emulsions, 0.2-2% in creams, 0.4-2% in linaments.
HEC	Free-flowing granular powder.	Completely soluble in hot and cold water, will tolerate small amounts of some organic solvents. (dissolve in water first, then add remaining ingredients).	✓	0.5-1% in conditioning products; 1% in shampoos; 1% in toothpastes; 0.5-1.5% in shaving gels.

*Note that HPC is available in various molecular weights.

After considering the information from Tables 7 and 8, it was decided that hydroxypropylcellulose would not be substituted by any of the alternatives listed, but instead HPC with a slightly higher molecular weight relative to that used in the original (2009) formulation was selected. The selected ingredient is J CS, which has a molecular weight of 140K. It has been suggested that HPC with a higher molecular weight posses better filming properties[4]. J refers to the HPC grade, while CS refers to the fact that it was developed for use in cosmetic products. The molecular weight of the original HPC used is 100K, which means that a slight increase in viscosity is expected for the modified formulations containing this particular molecular weight HPC (J CS). The film formed by HPC is said to be flexible, clear, thermoplastic and non-tacky, which meet the requirements relative to this study. The high molecular weight grades of HPC (also known as high viscosity types) are incorporated into formulations to function as thickeners and film formers, while the lower molecular weight grades confer excellent film forming properties. The lower grade HPC is therefore used to facilitate in the improvement of the original formulation. Incorporating a chemical which increases the viscosity of the formulation excessively may influence the film formed in a negative way. The idea is that the film should be as efficient as possible, without forming a visible film on the skin surface.

1.3.5. Coconut Oil (CDE)

Safety and Applications

Coconut oil is an emollient; the function of an emollient being that it softens and makes the stratum corneum more pliable through the hydration thereof[68]. This constituent does not influence the slow release properties of the original formulation since it is simply an emollient and does not have any film forming properties. It is known to exert its benefits on the skin barrier through improved repair and permeability properties. PubMed concluded the following from a study with patients suffering from xerosis: “Coconut oil is as effective and safe as mineral oil when used as a moisturizer”[69]. Coconut oil acts as an

occlusive, which prevents xerosis (due to TEWL) when used in conjunction with a humectant such as propylene glycol.

Therefore, coconut oil will not be replaced but used in the modified formulation as the emollient component.

1.3.6. Polyquaternium-10

Safety

According to Locchead et al. (1993)[20], polyquaternium-10 is considered safe for use.

Applications

This constituent is a substantivity polymer and may be replaced by polyquaternium-11 or used in combination with it. It is a cationic polymer used primarily for film forming[70]. It also functions as a thickener, surfactant and binder[70,71,72].

Mixtures of substantivity polymers such as the above-mentioned along with lubricating polymers (PVP, polyethylene oxide, polyvinylpyrrolidone/vinyl alcohol copolymer, vinyl alcohol, vinyl acetate polymers, and polyacrylamide) lead to the formation of an entangled mesh that can act to entrap the lubricant polymer. This type of film forming system accordingly acts to provide sustained protection/lubrication[73].

In accordance with published reports[73], the minimum level of film forming materials is about 0.6% by weight of the base composition.

Tables 9 and 10 summarize the properties and uses of the following filming forming agents:

- Polyquaternium-10
- Polyquaternium-11
- Polyquaternium-16
- Polyquaternium-24

Table 9: Applications of polyquaternium-10 and selected alternatives.

	Substantive conditioner	Thickener	Surfactant	Binder	Film Former
[70,71,72]Polyquaternium-10 (skin & hair)	✓	✓	✓	✓	✓
[71]Polyquaternium-11 (hair mostly)	Hair conditioner			✓	✓
[74]Polyquaternium-16 (hair mostly)	✓		✓		✓
[75]Polyquaternium-24 (skin and hair)	✓	✓	✓		✓

Table 10: Characteristics of Polyquaternium-10 and selected alternatives.

	Form (solid/liquid)	Compatibility & formulating considerations	Safety (CIR Expert Panel)	Suggested use
[20]Polyquaternium-10 Substantive to protein substances (such as skin and hair)	White, granular powder (cosmeticinfo.org) with characteristic amine odour	Soluble in both water and 50% aqueous ethanol. Compatible with anionic, amphoteric, non-ionic or cationic systems. Suitable for any conditioning requirement due to its formulation flexibility.	✓	0.3-1% in hair care lotions, gels, mousses as well as in cleansers; 0.2-1% in skin care products.
[20]Polyquaternium-11	Water or alcohol solution	Soluble in water and alcohol When making carbomer gels with this compound: ensure pH >5 to prevent incompatibilities.	✓	2-10% in mousse an gel formulations. 2-5% in conditioners and shampoos.
[20]Polyquaternium-16	Aqueous solutions of 40% solids except Luviquat HM-552 which is 20%	Soluble in both water and alcohol. Add to water when added to formulations.		3-4% in shampoos and conditioners.
[20,75]Polyquaternium-24 (Substantive to protein substrates where it forms a uniform film on hair/skin due to its balanced hydrophobic /hydrophilic structure	Powder	Soluble in water and hydroalcoholic systems up to 50% ethanol. Good compatibility with most personal care ingredients.	✓	0.2-0.5% in skin lotions or creams. 0.5-1.0% in shampoos and conditioning mousse products.

It was, however, concluded that polyquaternium-10 does not have to be replaced and can be used as is in the modified formulation, since polyquaternium-10 in itself seems to have more beneficial characteristics than any of the alternatives. None of the alternatives mirror polyquaternium-10 exactly, and none of them have additional properties which might strengthen the slow release characteristics of the original formulation. It will be interesting to note whether release properties will be modified when it is used with the PVP-K30 alternative, polyurethane-32 (Baycusan® C1003)[73].

1.3.7. Citroflex (Triethyl citrate)

Citroflex (a series of citric acid esters) is a safe to use (U.S. Food and Drug Administration) plasticizer, and is compatible with a number of frequently used polymers, where it reduces the hardness or brittleness of polymeric materials where flexibility is required[76]. Although a plasticiser was added, the effect of the plasticiser on the slow release properties of the fixative formulations was not the objective of this study. It was simply added to the fixative formulations to improve the suppleness of the films formed by the fixative formulations.

1.3.8. Summary of alternatives

To summarise; the following ingredients will be investigated as replacement constituents in the original formulation including upper and lower weight percentage limits. See Table 11 below.

Table 11: Original (2009) vs. alternative film forming ingredients.

Original ingredient	Alternative
Hydroxypropylcellulose 100K	Hydroxypropylcellulose 140K
Polyvinylpyrrolidone K-30	Polyurethane-32 (Baycusan® C1003)
PEG-12 Dimethicone (SF1288)	Cetyl Dimethicone (Dow Corning® 2502 Cosmetic Fluid)
Triethyl citrate	None
Coconut oil	None
Propane-1,2-diol/propylene glycol	None
Polyquaternium-10/Merquat10	None

The original ingredients will be substituted in an ordered fashion, facilitated by a statistically formulated experimental design in order to evaluate whether (a) an improved slow release formulation can be developed, and (b) whether the various experimental procedures (to be described) are suitable for such a study.

1.4. Problem statement

The scents and odours giving fragrances their unique qualities are short lived and dissipate within a matter of hours[3]. They are also removed prematurely through normal daily activities such as perspiring, washing or simply by wearing clothes[77]. The major challenge is therefore to create a slow release formulation which facilitates the prolonged activity of actives in a formulation without causing skin irritation.

1.5 Research hypothesis

The slow release effectiveness of the original (2009) fixative formulation can be improved by the careful replacement of fixative components in a designed experiment using the rate of active disappearance from a glass surface as a measure of effectiveness.

1.6. Aim / Objectives

The aims/objectives of the study are the following:

1. To investigate whether certain ingredients in the original perfume fixative formulation can be replaced by alternative, yet similarly acting components.
2. To investigate whether the effectiveness of “slow release" in the presence of a perfume fixative formulation can be measured effectively by the rate of evaporation of an “active” substance from a glass surface under controlled conditions.
3. To investigate whether the rate of evaporation can be used as an effective measure of “slow release”.
4. To investigate whether certain individual components can improve or worsen the effectiveness of the fixative formulation and can be identified in a designed experiment.

CHAPTER 2

EXPERIMENTAL

This chapter provides details of the materials used in the formulations and in the analysis of the formulations, as well as details of the relevant calculations and experimental procedures. All materials were used as received, unless otherwise indicated.

2.1 Materials

Table 12 lists the materials used for preparing fixatives and fragrance mixtures as well as material used for analyses.

Table 12: Materials

Name of Ingredient	Supplier	Grade
Part A: Materials for FORMULATIONS		
Polyquaternium-10 (Merquat 10)	NALCO	Cosmetic
Hydroxypropylcellulose140K (KLUCEL® J CS)	HERCULES	Cosmetic
Hydroxypropylcellulose 100K	ALFA AESAR	Laboratory
Polyurethane-32 (Baycusan® C1003)	BAYER MATERIALSCIENCE, via Savannah fine chemicals	Cosmetic
Polyvinylpyrrolidone K-30	AKULU CHEMICALS	Non-pharmaceutical
PEG-12 Dimethicone (SF1288)	BAYER: GE BAYER SILICONES	Laboratory
Cetyl Dimethicone (Dow Corning® 2502 Cosmetic fluid)	DOW CORNING CORPORATION	Cosmetic
Triethyl citrate (Citrofol® A1)	JUNGBUNZLAUER	Laboratory
Propane-1,2-diol	MINEMA	Laboratory
Coconut oil	Sharon Bolel Chemical Marketing	Cosmetic
Distilled water	NMMU	Laboratory
Part B: Materials for ANALYSIS		
Ethanol	EC LAB SERVICES	96-99.9% AR
Methyl Benzoate	BDH LABORATORY REAGENTS	Laboratory
4-methylbenzaldehyde, 98%	ALDRICH	Laboratory

2.2 Experimental Procedures

2.2.1 Preparation of fixative formulations

Eighteen fixative formulations were prepared according to a formulation sheet for each different fixative formulation (derived from an experimental design). A typical formulation sheet is illustrated in Table 14. Table 13 shows the preparation method for a 2% w/w polyquartenium-10 solution which was used in each formulation. Figure 1 shows a schematic diagram of the mixing equipment.

Table 13: Preparation of a 2 % w/w polyquaternium-10 solution.

Ingredient	**Mass (g)**
Polyquaternium-10	1
Distilled water	49
Total	50
METHOD	
Add 1 g Polyquaternium-10 to 49 g of water at room temperature and homogenize using IKA® T18 Ultra-Turrax (speed setting 2; 7000 rpm) homogenizer until clear (± 75 minutes).	

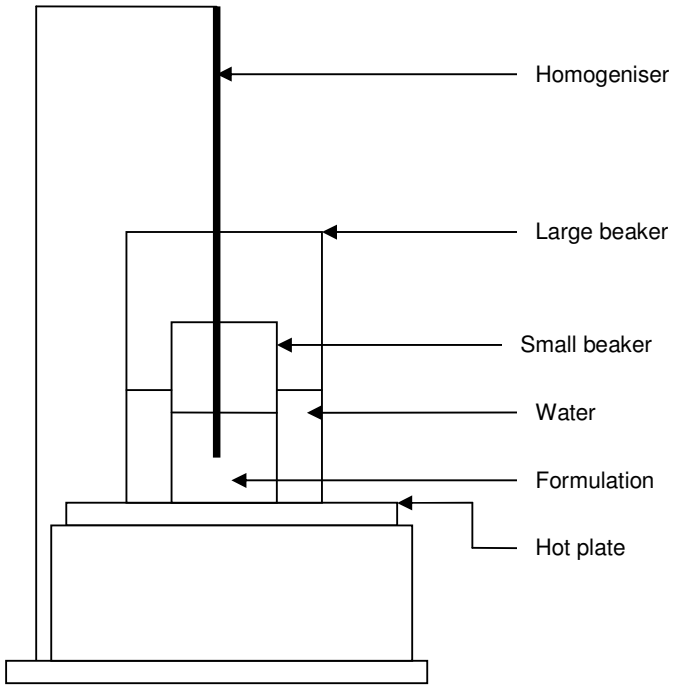

Figure 1: Schematic diagram of mixing equipment.

Table 14: Representative fixative formulation (formulation # 1).

Phase	Ingredient	Mass (g)	% w/w
A	Polyquaternium-10/DI water (from Table 13)	5.44	13.6
	PEG-12 Dimethicone	0.2	0.5
	Triethyl citrate	1.6	4
B	Hydroxypropylcellulose(100K)	0.4	1
	Hydroxypropylcellulose (140K)	2.0	5
	Propane-1,2-diol	26.43	66.1
	Polyurethane-32 (Baycusan® C 1003)	1.2	3
	Polyvinylpyrrolidone K-30	1.2	3
	Coconut oil	0.53	1.30
	Cetyl dimethicone	1.0	2.5
	Total mass:	40 g	100 %
METHOD			
Phase A (aqueous phase)			
To 5.44 g of the Polyquaternium-10 and DI water mixture, add 0.2 g PEG-12 dimethicone while stirring at room temperature. Add 1.6 g triethyl citrate to the mixture and stir (room temperature).			
Phase B (oil phase)			
Dissolve 0.4 g hydroxypropylcellulose (100K) in 26.43 g propane-1.2-diol and homogenize (3500 rpm when using the IKA® T18 basic, Ultra-Turrax homogenizer; at a low heat setting). Then add 2.0 g hydroxypropylcellulose (140K) to the mixture and homogenise using homogenizer (7000 rpm) while heating the mixture (low heat setting). To the homogenized mixture, add 1.2 g PVP and once again homogenize (7000 rpm) while heating. Then add 1.2 g polyurethane-32 and homogenize while heating. Add 0.53 g of molten coconut oil to the mixture and homogenize (7000 rpm). Once homogenized, add 1.0 g cetyl dimethicone, preheated to 40^{o} C, to the mixture and homogenise (7000 rpm) once again.			
Mix phases A and B using a homogenizer (7000 rpm), until the two phases are homogeneous.			

Formulation observations

Phase A

The starting point for this phase was making a 2 % solution of polyquaternium-10 and distilled water. Upon addition of distilled water to polyquaternium-10, small aggregates of the small powder granules formed. This mixture was homogenised at room temperature with the aid of the IKA® T18 Ultra-Turrax® homogenizer (7000 rpm). It took approximately 75 minutes for the solution to become clear. For the purpose of this study, a stock solution of this mixture was made and used throughout to minimize variation.

This solution was used over a 4 month period. During this period, no phase separation took place.

After the specified mass of the homogenized mixture was weighed off, PEG-12 dimethicone was added and the mixture was stirred using a glass rod. The mixture was clear with finely dispersed gas bubbles within. A plasticizer, Citroflex (as described in the ingredients section), was then added to the mixture and it was stirred well (as in the case with PEG-12 dimethicone). The mixture became murky and, once again, small air bubbles were dispersed within the homogenized mixture. No individual plasticizer droplets should be visible.

All of the ingredients in phase A were weighed into and mixed within a single beaker to avoid loss of the ingredients, since such small masses were weighed off.

Phase B

Hydroxypropylcellulose 100K and 140K were dissolved in propane-1,2-diol, with the aid of a water bath. When placed into a water bath, the beaker containing the mixture was placed into a larger beaker containing a small amount of water and placed on a hot plate and to allow the water in the larger surrounding beaker to heat. The IKA® T18 Ultra-Turrax homogenizer was used to homogenise the mixture (3500 rpm). Since HPC (hydroxypropylcellulose) 140K has a higher molecular weight relative to HPC 100K, the formulations containing more HPC 140K were denser than the ones containing a greater proportion of HPC 100K. The formulations containing more HPC 140K also did not become completely clear upon homogenization, but remained slightly murky. Murkiness was also attributed to the finely dispersed gas bubbles, which were formed while the mixture was homogenized. The rotor speed of the IKA® T18 Ultra-Turrax was 3500 rpm.

Once polyvinylpyrrolidone K-30 and polyurethane-32 (Baycusan® C 1003) were added to the HPC 100K/HPC 140K/propane-1,2-diol mixture, the mixture became even more viscous, and the rotor speed of the IKA® T18 Ultra-Turrax

had to be increased to 7000 rpm. Polyurethane-32 is a milky, sticky liquid which easily forms a film when it comes into contact with a glass or plastic surface.

Upon the addition of the melted coconut oil, an oily layer formed on the surface of the mixture. It is important to finely disperse the oil droplets; therefore it was mixed using the IKA® T18 Ultra-Turrax homogenizer (7000 rpm) until the mixture is completely homogeneous. Cetyl dimethicone was the last ingredient to be added to the formulation. It too had to be melted before it was incorporated into phase B of the formulation, since this aids in the formation of a homogeneous mixture. It also formed an oily layer on the surface. The suppliers suggest that cetyl dimethicone should be added to the oil phase of a formulation, which is why it was not added to phase A together with PEG-12 dimethicone. Homogeneity of phase B has to be ensured before mixing phases A and B.

As with phase A, extremely small amounts of the components or ingredients were weighed into a single container to avoid unnecessary loss.

Phase A and B

Although phase A is the lower volume phase, phase B (oil) was added to phase A (water), since addition in this fashion will lead to phase inversion. This results in better dispersion of the water droplets within the oil phase. This formulation can therefore be described as a water in oil emulsion. Once the two phases were added to one another, the mixture became murky white. It was mixed using the homogenizer, rotor speed of 7000 rpm.

2.2.2 Fragrance sample preparation

Once all of the fixative formulations were completed, fragrance samples were prepared for evaporation studies. For the purpose of this study, fragrance samples contained 8% fixative, 6% fragrance and 86% ethanol (weight percentage). These concentrations were selected to ensure miscibility of the components and the homogeneity of the solutions prepared for incubation.

The fragrance component was solubilised in the fixative formulation before ethanol was added to produce the incubation sample. It is important that the fragrance component forms a homogeneous mixture with the fixative component. The concentrations of the fragrance and fixative components have to be easily detectable since the incubated samples are analysed using a gas chromatograph. 4-Methylbenzaldehyde ($C_8H_8O_2$) was used during this study to "represent" a fragrance so as to simplify quantification by GC-analysis. 4-Methylbenzaldehyde is a simple molecule which is easily analysed using gas chromatography (GC). For this particular fragrance molecule, clear peaks were observed at a retention time of ± 10.4 minutes and no interference with the peak areas of any other components within the formulation were observed when injected into the GC for analysis. The evaporation rate of this fragrance molecule over time relative to 18 different fixative formulations was evaluated in an effort to determine which of the components or ingredients in the fixative formulations most significantly reduces its evaporation rate.

2.5 g samples were prepared as follows: A constant amount (ca. 0.2 g) of each respective fixative formulation was weighed accurately into a pill vial, followed by 0.15 g of the fragrance (4-methylbenzaldehyde). The pill vial was kept closed to prevent evaporation of the fragrance components as it was weighed off. These two ingredients were thoroughly mixed after which ca. 2.15 g ethanol was weighed into the same container and stirred (magnetically) for ± 4 minutes until the mixture was completely homogeneous.

2.2.3 Evaporation studies

All evaporation studies were carried out in an environmental room under constant environmental conditions of temperature (28 °C – 29 °C) and air flow. For each fragrance sample, six petri dishes (diameter of 50 and 55 mm) were allowed to equilibrate to the environmental room conditions for 24 hours. To each of the six petri dishes was added a fixed volume (0.076 ml) of an individual fragrance mixture using a 100 µl micropipette, dispersing the sample across the surface of the petri dish by gently tilting it, avoiding

spillage. Samples were left to evaporate in the environmental room for the desired times (0, 1, 2, 3, 4, and 5 hours, respectively), after which the petri dishes were rinsed 3 times with an ethanol solution containing a known amount of methyl benzoate (GC internal standard – 0.85 g/L), transferring the washings quantitatively into a 10 mL volumetric flask and making up to volume. Note that these preliminary trials (over 5 hours) were conducted to establish which of the fixative formulations facilitated the slow release of the fragrance component for a period exceeding 5 hours. This was done in an effort to save some time, since this study is time-dependent. Aliquots of the well mixed analysis samples from the volumetric flasks were then transferred to GC vials and analysed as described below.

Ethanol was used as a solvent for both the fixative/fragrance formulation (which is incubated) and for the internal standard stock solution. Analar grade ethanol was used to prevent any kind of contamination relative to the internal standard and active peaks (GC analyis).

2.2.4 Analytical method

2.2.4.1 Gas Chromatography method

Fragrance samples were analysed by gas chromatography (Agilent Chemstation 6850, fitted with an FID detector, autosampler, and linked to a personal computer with Chemstation software). The following GC method was used for the quantification of 4-methylbenzaldehyde during this study:

Injection volume	: 1µl
Initial column temperature	: 80 ℃
Initial hold time	: 2 minutes
Heating rate	: 15 ℃/minute
Final column temperature	: 240 ℃
Final hold time	: 5 minutes
Column	: HP5MS (29.9m x 250µm x 0.25µm)
Injector temperature	: 250 ℃

Detector temperature : 300 ℃

2.2.5 Calculations

2.2.5.1 Calculations and method evaluation

The concentration of 4-methylbenzaldehyde was determined in fragrance samples using the internal standard method and using methyl benzoate as the internal standard. The relative response factor for 4-methyl benzaldehyde was calculated over a pre-determined concentration range of the active using equation 2.1. The response factor must remain constant over the concentration range used.

$$RF = \frac{(C_a \cdot A_{is})}{(A_a \cdot C_{is})} \qquad \text{(Eqn. 2.1)}$$

Where:

RF : Response Factor;

C_a : Concentration of the active (g/L);

A_{is} : Peak area of the internal standard;

A_a : Peak area of the active;

C_{is} : Concentration of the internal standard (g/L).

The fragrance (4-methylbenzaldehyde) and internal standard (methyl benzoate) had retention times of ±7 and ±5 minutes, respectively. This implies that the peaks are clearly defined and distinguished from one another and that no overlapping of peak areas occurs.

To determine the response factor, four solutions of the fragrance (4-methylbenzaldehyde) in the concentration range 1.1-1.3 g/L (using a constant amount of 1.7 g/L methyl benzoate in ethanol) were prepared and analysed by GC in triplicate. Table 15 summarises the results obtained.

Table 15: Determination of the relative response factor for 4-methylbenzaldehyde.

Concentration (g/L)	$RF=(A_{is}*C_a)/(C_{is}*A_a)$ Response factor
1.1	1.16867
1.1	1.15589
1.1	1.15729
1.15	1.16782
1.15	1.15855
1.15	1.17013
1.2	1.16023
1.2	1.15861
1.2	1.15887
1.3	1.15847
1.3	1.13979
1.3	1.14376
	Ave = 1.158173

2.2.5.2 Calculation of fragrance concentration

The concentrations of fragrance in samples were calculated using equation 2.2:

$$Ca = \frac{(RF \cdot C_{is} \cdot A_a)}{A_{is}} \qquad \text{(Eqn. 2.2)}$$

Where:

C_a : Concentration of the active;

RF : Response factor;

C_{is} : Concentration of the internal standard;

A_a : Peak area of the active;

A_{is} : Peak area of the internal standard.

The concentration of the active and internal standard is reported in g/L.

2.2.6 Evaporation study – method validation

The repeatability of the evaporation methodology was confirmed through a replicated experiment. Three replicated samples were prepared as in section 2.2.2 and allowed to evaporate before analyzing by GC. Table 16 lists the masses of the components used to compare the replicate fragrance samples, while Table 17 lists the masses of the aliquots of the evaporated fragrance samples prepared as in section 2.2.3. Table 18 summarizes the results of the GC analyses for this validation study.

Table 16: Masses of the components used to prepare replicate fragrance samples for validation study (total sample mass10 g).

	Mass (g)		
Run	**Active (6%)**	**Fixative (8%)**	**Ethanol (86%)**
1	0.6006	0.8021	8.6095
2	0.6013	0.8021	8.6078
3	0.6009	0.8015	8.6096

Table 17: Masses (g) of aliquots from replicate samples used in evaporation study.

	Mass (g)		
Run	**0 hr**	**3 hr**	**6 hr**
1	0.2175	0.2171	0.2165
2	0.2167	0.2171	0.2176
3	0.2170	0.2173	0.2175

Table 18: Summary of GC results – evaporation method validation study.

Run	Time (hr)	Calculated C_a (g/L)	C_{is} (g/L)	Response Factor
1	0	1.365	1.702	1.158
	3	0.751		
	6	0.000		
2	0	1.339		
	3	Spilled		
	6	0.000		
3	0	1.338		
	3	0.756		
	6	0.000		

The three sets of data tabulated in Table 18 were compared to one another using a dummy regression analysis (description below). The design is shown in Table 19. To accomplish this, the first run has to be compared to both runs 2 and 3 and run 2 has to be compared with run 3. This will then facilitate in the comparison of all three of the data sets to one another. This was however accomplished with a single regression analysis.

Table 19: Dummy regression analysis design.

Run #	Time (hours)	D_1	D_2	D_1*Time	D_2*Time	C_a (g/L)
1	0	0	0	0	0	1.365
	3	0	0	0	0	0.751
	6	0	0	0	0	0
2	0	1	0	0	0	1.339
	6	1	0	6	0	0
3	0	0	1	0	0	1.338
	3	0	1	0	3	0.756
	6	0	1	0	6	0

The model is as follows:

$$\hat{C}_a = b_0 + b_1*\text{Time} + b_2*D_1 + b_3*D_2 + b_4*D_1*\text{Time} + b_5*D_2*\text{Time} \qquad \text{(Eqn. 2.3)}$$

Where:

$\hat{C}_a$: Estimated concentration of the fragrance (g/L) after the stipulated time interval;

b_x : Coefficients of various factors;

D_x : Binary dummy variable;

Run 1

The following is assumed: $D_1 = D_2 = 0$. These values are then incorporated into equation 2.3 above and the following equation is obtained for run 1:

$\hat{C}_a = b_0 + b_1*\text{Time} + b_2*(0) + b_3*(0) + b_4*(0)*\text{Time} + b_5*(0)*\text{Time};$

This simplifies to:

$\hat{C}_a = b_0 + b_1*\text{Time}$ (Eqn. 2.4)

Run 2

The following is assumed: $D_1 = 1$ and $D_2 = 0$. These values are substituted into equation 2.3 and the following equation is obtained for run 2:

$\hat{C}_a = b_0 + b_1*\text{Time} + b_2*(1) + b_3*(0) + b_4*(1)*\text{Time} + b_5*(0)*\text{Time};$

This simplifies to:

$\hat{C}_a = (b_0+\mathbf{b_2}) + (b_1+\mathbf{b_4})*\text{Time}$ (Eqn. 2.5)

Comparing run 1 to run 2: If $\beta_2 = 0$ then the data points at time zero will be going through the same point (initial concentrations will be equal to one another). This is a positive effect.

If $\beta_4 = 0$, it means that the gradient of run 1 is equal to that of run 2 and that there is no significant difference between the rate of loss of the fragrance in run 1 relative to run 2. In this case, we want to prove that run 1 = run 2 = run 3.

Note that the symbol $\boldsymbol{\beta}$ represents the true coefficient and that $\boldsymbol{b}$ represents the estimated coefficient, where b is a sample-dependant statistic.

Run 3

The following is assumed: $D_1 = 0$ and $D_2 = 1$. These values are substituted into eqn. 2.3 and the following eqn. is obtained from run 3:

$\hat{C}_a = b_0 + b_1*\text{Time} + b_2*(0) + b_3*(1) + b_4*(0)*\text{Time} + b_5*(1)*\text{Time};$

This simplifies to:

$\hat{C}_a = (b_0+\mathbf{b_3}) + (b_1+\mathbf{b_5})*\text{Time}$ (Eqn. 2.6)

Comparing run 1 to run 3: If $\beta_3 = 0$ then it once again implies that the initial concentration of runs 1 and 3 is identical to one another, which is a positive result. If $\beta_5 = 0$, then it implies that the gradient of run 3 is equal to that of run 1 and that there is no significant difference between the rate of loss of the fragrance in run 1 relative to run 3. For the purpose of this method validation, it is crucial that b_4 and b_5 are both equal to zero to prove that the method is repeatable.

A regression analysis was carried out (using Table 19), where the y-values inserted were the fragrance concentrations, C_a (g/L) after stipulated incubation periods. The x-values inserted into the data analysis program came from the rest of Table 19, namely , D_1, D_2, D_1*Time and D_2*Time. The regression results obtained are shown in Table 20.

Table 20: Regression output for dummy regression analysis.

SUMMARY OUTPUT						
Regression Statistics						
R Square	0.997016					
Adjusted R Square	0.989556					
Observations	8					
ANOVA						
	Coefficients	*Standard Error*	*t Stat*	*P-value*	*Lower 95%*	*Upper 95%*
Intercept	1.387916	0.05829	23.81038	0.001759	1.137113	1.638719
Time	-0.68251	0.045152	-15.116	0.004348	-0.87678	-0.48824
D1	-0.04934	0.086459	-0.57063	0.625817	-0.42134	0.322666
D2	-0.02071	0.082435	-0.25128	0.825061	-0.3754	0.333975
D1*Time	0.013222	0.063854	0.207068	0.855126	-0.26152	0.287963
D2*Time	0.01336	0.063854	0.20923	0.853645	-0.26138	0.288101

The p-values associated with the null hypotheses that $\beta_4 = 0$ and $\beta_5 = 0$ are greater than 0.05, thus the null-hypothesis is accepted. This implies that the gradients of runs 2 and 3 are equal to that of run 1 and that there is no significant difference between the rates of loss of the fragrance between these three runs. The p-values associated with the null hypotheses that $\beta_2 = 0$ (run 2) and $\beta_3 = 0$ (run 3) are also greater than 0.05, thus the null hypothesis is accepted, proving that runs 2 and 3 have the same intercept or initial concentration as run 1.

The method is therefore proven to be valid, since the gradients and intercepts of the three runs respectively, are equal to one another.

CHAPTER 3

EVALUATION OF FIXATIVE FORMULATIONS

This chapter describes the methodology, results, and the analysis of the results pertaining to the research hypothesis stated in chapter 1: the slow release effectiveness of a typical perfume fixative can be improved by the careful replacement of fixative components in a designed experiment using the rate of active disappearance from a glass surface as measure of effectiveness. In order to prove or disprove this hypothesis, a statistically designed experiment was used to determine which of the ingredients in the fixative formulations influences the rate of loss of fragrance compound, and in what manner (namely, increased or decreased rate of evaporation). The data from the evaporation studies described in Chapter 2 was first modelled by fitting an exponential curve to the data, after which multiple linear least squares regression was used to derive a response surface model that describes the variation in results as a function of the individual fixative components. The latter model was analysed in detail using statistical methods in order to show that the model so derived is valid.

3.1 Formulation constraints

Certain constraints had to be enforced in terms of the minimum and maximum percentage of each ingredient in the formulations in order to allow the interpretation of results in terms of the nature of the ingredients only. This implies that the total amount of fixative ingredients was always constant, and in fact, groups of ingredients (see Table 22) were also constant. It should therefore be noted that the aim was to identify which ingredients influenced “slow release” and not necessarily to find the optimum concentration of ingredients in an ideal fixative formulation. Table 21 summarises the details of the fixative formulations showing the various groups of ingredients and the upper and lower limits for the groups of ingredients.

Table 21: Fixative formulation details (upper and lower limits).

Chemical name	Lower Limit (wt. %)	Upper Limit (wt. %)	Notes (for a total mass of 40 g)
Variables			
HPC (100K) **HPC (140K) (JCS)**	0 0	6 6	HPC (100K) functions as a film former, emulsion and foam stabiliser, thickener, binder and rheology modifier. HPC (140K) acts as a film former and thickener. HPC (100K) together with JCS (group 1) add up to 2.4 g (6% of the formulation).
PVP-K30 **Polyurethane-32 (Baycusan C1003)**	0 0	6 6	In the cosmetic industry PVP functions as a filming agent, thickener, lubricant and adhesive. Baycusan C1003 is a film former and lubricant. PVP and Baycusan C1003 (group 2) together add up to 2.4 g in total (6% of the formulation).
PEG-12 Dimethicone (SF1288) **Cetyl Dimethicone (DC 2502)**	0 0	3 3	PEG-12 dimethicone functions as a film forming agent, emollient, lubricant and provides substantivity and wash-off resistance. Cetyl dimethicone provides moisturization and is substantive to skin. SF1288 and cetyl dimethicone (group 3) add up to a total of 1.2 g (3% of the final formulation).
Constants			
Citroflex (plasticizer)	4	4	Citroflex is a plasticizer which facilitates in the formation of a flexible film. A total of 1.6 g (4%) citroflex is present in each formulation.
Coconut oil	1.32	1.32	Coconut oil primarily functions as an emollient and a total of 0.53 g (1.32%) of this ingredient is present in each formulation.
Propane-1,2-diol	66.1	66.1	This ingredient is the primary solvent for HPC (100K) and HPC (140K). It also functions as a humectant in the formulations; a total of 26.43 g (66%) is present in each formulation.
Polyquaternium-10/water (98:2)	13.6	13.6	Polyquaternium-10 is a substantivity polymer, also acting as a thickener and surfactant and binder. A total of 0.27% (2 g polyquaternium-10 in 98 g water) polyquaternium-10 is present in the formulation. 13.6% (5.440 g) of the polyquaternium-10/water mixture is present in the final formulation.

From Table 21 above it should be noted that the selected lower limit of the various ingredients with their alternatives is 0 %. This is because the effect of each ingredient in the absence of the alternative ingredient was also investigated. Note that the fixative formulations prepared are incorporated as small fractions (8%) of the fragrance samples (refer to section 2.2.2 in Chapter 2), which means that the final concentrations of the ingredients in Table 21 will be significantly less than recommended by the suppliers. Such small concentrations were used to ensure homogeneity between the fragrance component, fixative formulation and ethanol. Without homogeneity, the evaporation rate may be adversely affected[5]. Certain sources state that even low concentrations of fixative formulations decrease the rate at which the fragrance component evaporates[4].

3.2 Fixative Formulation Evaluations

3.2.1 Details of the experimental design

A two level factorial design was selected since it aids in the evaluation of the combined effects of various factors on the selected response.

Table 22: Two-level factorial design details.

	Mass of variable ingredients (g)						
	A	**B**	**C**	**D**	**E**	**F**	
Formulation	HPC (100K)	HPC (140K)	PVP-K30	Polyure-thane-32	PEG-12 dimethicone	Cetyl dimethicone	**Total**
1	0.4	2	1.2	1.2	0.2	1	6
2	0.4	2	0.4	2	0.6	0.6	6
3	0.4	2	2	0.4	1	0.2	6
4	1.2	1.2	2	0.4	0.2	1	6
5	0.4	2	0.4	2	1	0.2	6
6	2	0.4	0.4	2	1	0.2	6
7	2	0.4	2	0.4	1	0.2	6
8	0.4	2	0.4	2	0.2	1	6
9	1.2	1.2	0.4	2	0.2	1	6
10	2	0.4	0.4	2	1	0.2	6
11	0	2.4	2.4	0	0.6	0.6	6
12	2.4	0	2.4	0	0.6	0.6	6
13	2.4	0	0	2.4	0.6	0.6	6
14	0	2.4	0	2.4	0.6	0.6	6
15	1.2	1.2	1.2	1.2	1.2	0	6
16	1.2	1.2	1.2	1.2	0	1.2	6
17	1.2	1.2	1.2	1.2	0.6	0.6	6
18	1.2	1.2	1.2	1.2	0.6	0.6	6

Note that the variable ingredients in each of the formulations (1-18) add up to a total of 15% of the overall formulation (40 g).

3.2.2 Results from evaporation studies

Fixative formulations were prepared using each of the mixtures (1-18) listed in Table 22 together with the constant ingredients listed in Table 21 and using the method of preparation described in section 2.2.1 in Chapter 2. The

fragrance samples were then prepared according to section 2.2.2 and subjected to evaporation as described previously. The results obtained from the GC analysis are summarised in Table 23.

Table 23*:* Results from the evaporation studies conducted over a total period of 5 hours.

Time (hr)	0	1	2	3	4	5
Formulation	**Fragrance Concentration (g/L)**					
1	0.466	0.221	0.144	0.057	0.055	0
2	0.431	0.236	0.16	0	0	0
3	0.425	0.307	0.19	0.149	0	0
4	0.509	0.276	0.223	0.111	0	0
5	0.501	0.263	0.187	0.083	0.047	0
6	0.519	0.199	0.141	0.074	0	0
7	0.52	0.254	0.095	0.081	0	0
8	0.533	0.265	0.198	0.062	0	0
9	0.517	0.306	0.148	0.112	0	0
10	0.522	0.221	0.153	0.076	0	0
11	0.367	0.202	0.155	0.06	0	0
12	0.365	0.252	0.187	0.046	0	0
13	0.369	0.241	0.177	0.067	0	0
14	0.361	0.248	0.166	0.047	0	0
15	0.37	0.256	0.156	0.045	0	0
16	0.358	0.264	0.17	0.058	0.056	0
17	0.362	0.243	0.163	0.048	0	0
18	0.376	0.255	0.113	0.088	0	0

The results above show that, as expected, the effect of the fixative on the rate of evaporation is quite small as none of the fragrance samples retain any of the fragrance compound after 5 hours in the environmental chamber. This is probably due to the fact that the film forming ingredients in the fixative formulation were deliberately kept at a low weight percentage (to ensure homogeneity with the fragrance component and ethanol). In order to discern whether any differences exist between the various fixative formulations, the evaporation data in Table 23 was first fitted to a common evaporation model.

Unfortunately, none of the fixative formulations managed to release the fragrance at a low enough rate for it to meet the criteria set initially. Most of the fragrance samples evaporated completely (or a concentration of fragrance below the limit of detection of the GC was left behind) by the 5th hour of incubation.

3.2.3 Curve Fitting

The normal evaporation of a compound depends on various physical and chemical properties, as well as environmental factors including its boiling point, concentration, vapour pressure, viscosity, as well as temperature and air flow. Since evaporation studies were conducted under constant environmental conditions, it is reasonable to assume that the rate of evaporation would only depend on the concentration of the compound at any given time, as well as the kinetic energy of individual molecules to overcome the liquid-phase intermolecular forces. Since evaporation is essentially a phase transition occurring only on the uppermost surface layer of the liquid, a disturbance of this surface layer, for example by film formation, would directly influence the rate of evaporation. Assuming no physical interference, it is reasonable to assume that the rate of evaporation will be described by the following negative exponential model:

$$C = Y_0 e^{kt} + \varepsilon \qquad \text{(Eqn. 3.1)}$$

where:

C : Observed fragrance concentration at a given time t (g/L);

Y_0 : Initial Fragrance concentration (g/L);

k : Rate constant; and

ε : Residual;

e : Natural logarithm.

If the model presented by Equation 3.1 fits the observed data well, the residuals will be normally distributed and will have an average of zero.

The curve fitting was done using the Statistica[a] software package and the results are outlined in Table 24 below.

Table 24: Summarised model fitting results.

Formulation #	Y_0 (g/L) (p-value)	k (p-value)
1	0.461 (0.000017)	-0.652 (0.000224)
2	0.441 (0.000386)	-0.685 (0.004813)
3	0.445 (0.000613)	-0.471 (0.006274)
4	0.511 (0.000248)	-0.555 (0.002780)
5	0.499 (0.000020)	-0.581 (0.000242)
6	0.511 (0.000064)	-0.780 (0.000993)
7	0.523 (0.000018)	-0.765 (0.000287)
8	0.535 (0.000102)	-0.652 (0.001300)
9	0.526 (0.000066)	-0.613 (0.000818)
10	0.516 (0.000047)	-0.729 (0.000679)
11	0.371 (0.000171)	-0.584 (0.001996)
12	0.384 (0.000780)	-0.528 (0.007952)
13	0.383 (0.000374)	-0.528 (0.004017)
14	0.379 (0.000458)	-0.546 (0.004913)
15	0.388 (0.000362)	-0.562 (0.003990)
16	0.376 (0.000226)	-0.477 (0.002463)
17	0.378 (0.000378)	-0.553 (0.004126)
18	0.390 (0.000199)	-0.572 (0.002285

Note that the negative sign in front of the absolute k-value is purely indicative of the direction of the slope. This implies that the fragrance concentration decreases by the k-value every hour.

The null hypothesis associated with the k-values states that the true gradient, which represents the rate of loss of the fragrance, is zero. This implies that the fragrance concentration does not decrease over time. The alternative hypothesis states that the concentration of the fragrance component decreases over time. The null hypothesis associated with the true initial concentration (Y_0) of the fragrance, states that this concentration should be equal to zero while the alternative hypothesis states that the true initial concentration of the fragrance is not equal to zero.

The p-value associated with the null hypotheses gives the probability of a Type 1 error. A Type 1 error is rejecting the null hypothesis when it should have been accepted. It is customary to reject, the null hypothesis when the p-value associated with it, is lower than 0.05.

The p-values associated with both Y_0 and k for each of the formulations shown in Table 24 are however lower than 0.05 and the null hypothesis in both cases is rejected. This implies that the initial fragrance concentration is not equal to zero and the concentration of the fragrance decreases over time.

Figures 2 and 3 illustrate the results of the curve fitting for formulations 1 and 2 (actual data = points; predicted data = line). It simplifies the comparison of the observed and predicted values. It also confirms that the model fits the data points well, and can thus be used to interpret the results of this study. The curve fitting results for formulations 3 to 18 are available in Appendix B.

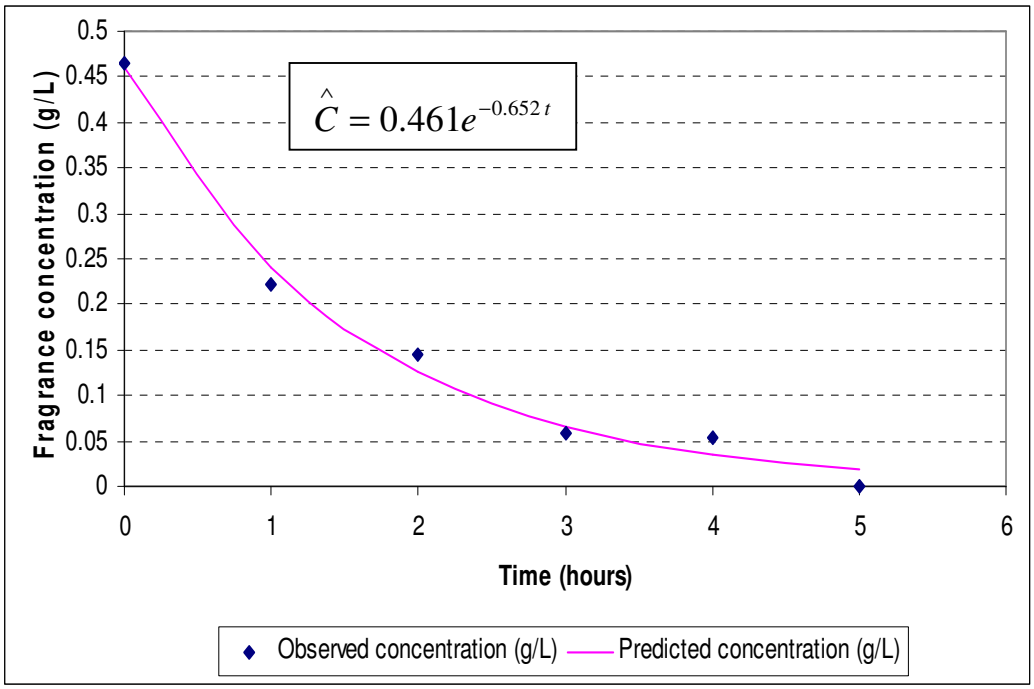

Figure 2: Results of curve fitting for formulation 1.

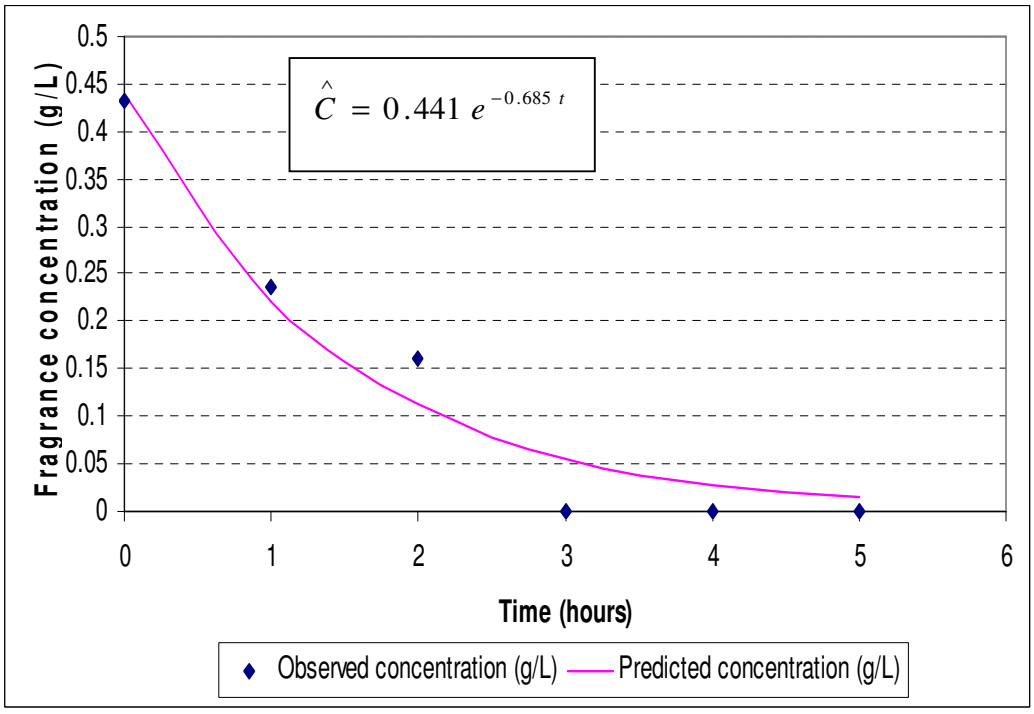

Figure 3: Results of curve fitting for formulation 2.

3.2.4 Calculation of fragrance half life

The rate constant is derived from the curves fitted to each one of the datasets and is represented by the symbol 'k' (as in Table 24). Each data point in Table 23, representing the samples incubated for different periods of time, is used to model the rate of loss of the fragrance per hour. The information gathered from all of the data points is then summarised by the rate constant, which is unique for each formulation and can therefore be used to compare the various formulations to one another. The rate constant indicates the rate at which the fragrance concentration (g/L) decreases per hour.

Now that the rate constant is known, the half life of the fragrance can be calculated. The half life of a fragrance is defined as the amount of time required for the fragrance (in this case) to evaporate to half of its initial concentration. The half life of the fragrance is calculated from the following equation:

$$\frac{1}{2}Y_0 = Y_0 e^{k\,t_{1/2}} \qquad \text{(Eqn. 3.2)}$$

Where:

$\frac{1}{2}Y_0$: Half of the initial fragrance concentration (g/L);

Y_0 : Initial fragrance concentration at time t (g/L);

$t_{1/2}$: Half life of the evaporating fragrance (hr);

k : Rate constant; and

e : Natural logarithm.

With some algebraic manipulation of equation 3.2, the half life of the fragrance can be calculated (equation 3.3)

$$t_{1/2} = \frac{-\ln(2)}{k} \qquad \text{(Eqn. 3.3)}$$

The results of the calculated half lives of the various formulations from the rate constants (from Table 24) are summarised in Table 25 below.

Table 25: Estimated fragrance half lives.

Formulation	Rate constant (k)	Half life (hours)
1	-0.65	1.06
2	-0.68	1.01
3	-0.47	1.47
4	-0.56	1.25
5	-0.58	1.19
6	-0.78	0.89
7	-0.77	0.91
8	-0.65	1.06
9	-0.61	1.13
10	-0.73	0.95
11	-0.58	1.19
12	-0.53	1.31
13	0.53	1.31
14	-0.55	1.27
15	-0.56	1.23
16	-0.48	1.45
17	-0.55	1.25
18	-0.57	1.21

The purpose of the study is to investigate the effect of the components in the various formulations on the rate of loss of the fragrance. The component which contributes most significantly to the reduction in fragrance loss over time is what is sought after. The smallest possible rate constant is therefore what is required to achieve this goal. As seen in equation 3.3, the half life of the evaporating fragrance is derived from the rate constant. When investigating the effects of the components on the evaporation rate of the fragrance in terms of its half life, the longest possible half life is desired.

Some variations in the rate constants and half lives of the 18 formulations were observed (Table 25). The lowest rate of fragrance loss was reported for formulation 3 (-0.47 g/L per hour). In contrast, the highest evaporation rate was associated with formulation 6, where 0.78 g/L of the fragrance evaporates hourly.

Mirroring these results, the half life of formulation 3 was 1.47 hours, while the shortest half life was 0.89 hours (formulation 6). It seems as if there is a difference between the minimum and maximum rate constants observed;

whether the "slow release" properties of formulation 3 are truly superior to those of formulation 6, should be statistically investigated.

3.2.5 Response Surface Modelling

3.2.5.1 Purpose

The primary purpose of modelling is to establish which one of the 6 components, as outlined in the design (Table 22), results in the observed variation in fragrance loss within the various fixative formulations (as seen in Table 25 above). This will facilitate in the identification of the components which most significantly influence the "slow release" properties of the fixative formulations.

3.2.5.2 Method

To identify the components which have a significant influence on the rate constant, the following multiple regression model was fitted:

$$k = b_0 + b_1 X + b_2 Y + b_3 Z + b_4 XZ + b_5 XY + b_6 YZ \qquad \text{(Eqn. 3.4)}$$

Where:

k : is the estimated rate constant; and

b_i : are the estimated coefficients (i=1,2,…,6).

Due to the fact that the sum of the components (the original with its alternative) is constant the factors are discussed as 3 groups, instead of 6 individual components. The letter X is representative of components A and B (A-B), Y of components C and D (C-D) and Z of components E and F (E-F), where: A = HPC (100K); B = HPC (140K); C = PVP-K30; D = Baycusan C1003; E = SF1288; and F = Cetyl Dimethicone.

General least squares regression was used to determine the estimated coefficients, b_i (where b_i, i = 1, 2, 3, 4, 5, 6). Regression analysis was

performed using the statistical software package Design-Expert (version 5.0.9)[b].

3.2.5.3 Results

The results of the linear least squares regression (using the rate constant data from Table 25), are summarised in Table 26.

Table 26: Summary of regression results – Rate constant.

Factor	Coefficient Symbol	Coefficient Estimate	Prob > |t|
Intercept	b_0	-0.81613	
X	b_1	0.249732	0.0013
Y	b_2	0.0208628	0.4446
Z	b_3	0.351164	0.0027
XZ	b_4	-0.013235	0.6156
XY	b_5	-0.00578948	0.7415
YZ	b_6	-0.382654	0.0004

3.2.5.4 Derivation and validation of response surface models

Having calculated values for the estimated coefficients does not imply that the true coefficients differ significantly from zero. Using a process of backward regression (namely, eliminating the coefficient with the largest p-value and re-calculating the coefficients and their p-values for the remaining coefficients until only statistically significant terms remain – i.e. coefficients whose associated p-values ≤ 0.05) results in the response surface models for the evaporation rate constant represented by equation 3.5. Table 27 summarises the Analysis of Variance for this "rate constant" model

$$k = b_0 + b_1 X + b_3 Z + b_6 XZ \qquad \text{(Eqn. 3.5)}$$

Equation 3.5 represents the final model for the estimated rate constants.

Table 27*:* ANOVA for "Rate constant" model.

Source of variation	Sum of Squares	Degrees of Freedom	Mean Square	F-Value	Prob > F (p-value)
Model	0.102363	3	0.034121	12.4766	0.0003
Residual	0.0382871	14	0.002735		
Lack of Fit	0.0368371	12	0.00307	4.23415	0.2068
Pure Error	0.00145	2	0.000725		
Cor Total	0.14065	17			
Factor	**Estimated Coefficient (b)**	**DF**	**t-value**	**Prob > |t|**	
Intercept	b_0 = -0.813796	1			
X	b_1 = 0.249343	1	4.94836	0.0002	
Z	b_3 = 0.364776	1	4.36165	0.0007	
XZ	b_6 = -0.390925	1	-5.65581	< 0.0001	
R-Squared	0.727784				

3.2.5.5 Interpretation of the models

The small p-value associated with the model (p = 0.0003) implies that the components have a significant effect on the rate constant. The lack of fit test, proves that the model fits the observed data well (p = 0.2068) and the R-squared value (0.73) suggests that 73% of the variation observed in the data is explained by the model.

When discussing the results in terms of the coefficients (and associated p-values) for each component, it is important to remember that component A is directly linked to component B due to the fact that the sum of A and B was kept constant (as described in section 3.2.5.2). This also applies to components C, D, E and F. The results are therefore discussed in terms of the following terms: X, Y and Z (representing components A and B, C and D, E and F respectively).

It appears as if an increase in the concentration of component X (where the effects of all the other components are kept constant) will have a beneficial effect on the rate of fragrance loss (b_1 = +0.25; p =0.0002), resulting in a lower rate of fragrance loss over time. This is because according to equation 3.5,

the rate of fragrance loss becomes less negative and closer to 0 by the contribution of combined component X. The same can be said for component Z. An increase in the concentration of component Z in the formulation, when keeping the concentrations of the other components constant, results in a decrease in the rate of fragrance loss (b_3 = +0.36; p = 0.0007). Increasing the concentrations of these two components should therefore improve the "slow release" properties of the fixative formulations.

A statistically significant interaction (p <0.0001) has taken place between components X (A-B) and Z (E-F), when the concentration of all the other components was kept constant. The interaction can be defined as follows: The effect of component X on the rate constant is modified when the concentration of component Z is increased. The negative coefficient of 0.391 associated with interaction XZ, will further decrease the centre point coefficient value of -0.814; negatively impacting the "slow release" properties of the fixative formulations. Therefore, when the concentrations of these two components are increased, the interaction will result in a larger negative rate constant and therefore a higher rate of evaporation.

This effect is however not as pronounced as the combined effects of components X and Z, and is masked by the positive effects that these components have on the rate of fragrance loss over time.

The coefficient of component Y (C-D) is not statistically significant (p>0.05), therefore increasing the concentration of this components does not improve the "slow release" properties of the fixative formulations. However, if components Y (C-D) should be excluded from the fixative formulations, the resultant "slow release" properties of these formulations may improve, since the effects of the remaining components (A-B) and (E-F) will be more pronounced because their relative concentrations will be greater. To test whether this assumption is true, components C and D should be excluded from the fixative formulation and evaporation studies should be conducted.

Further model validation

Further model validation was done by plotting the normal percentage probability against the studentized residuals to see whether the data followed a normal distribution or not. See Figure 4. An outlier T plot against experimental run number was also plotted to detect whether any data points were outliers. The outlier plot is shown in Figure 5.

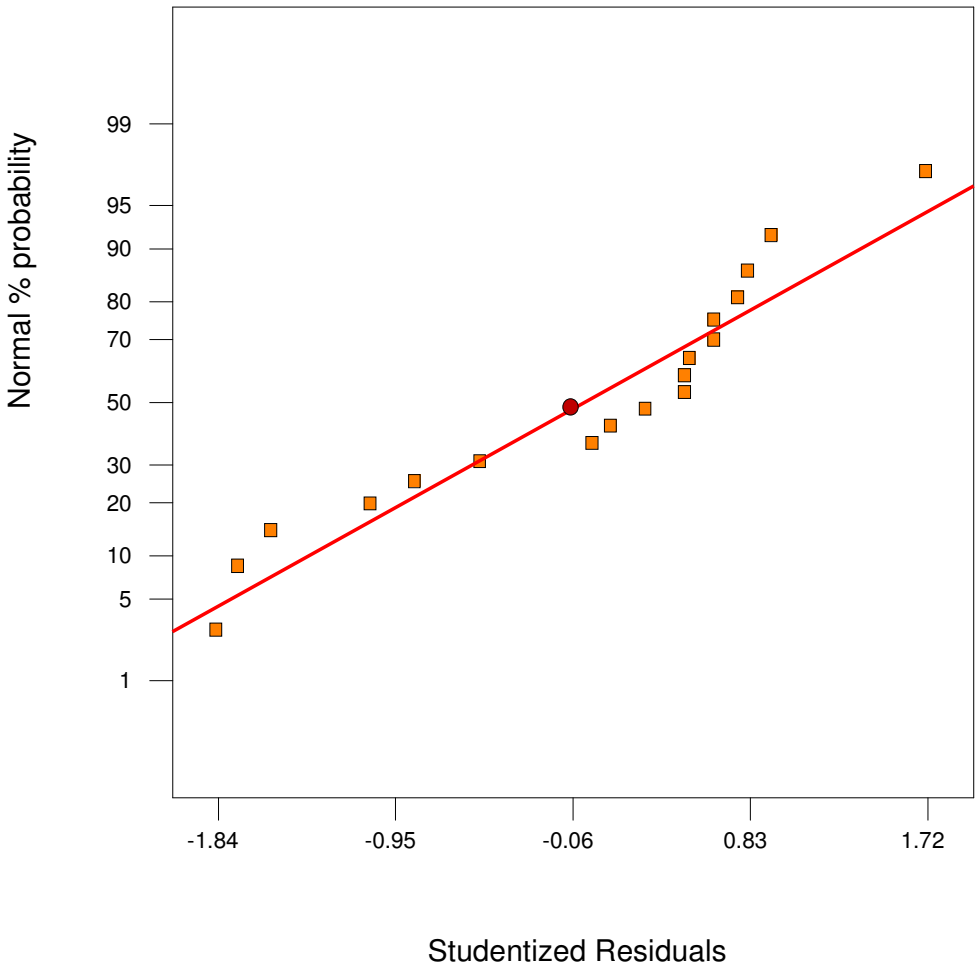

Figure 4: Normal plot of residuals.

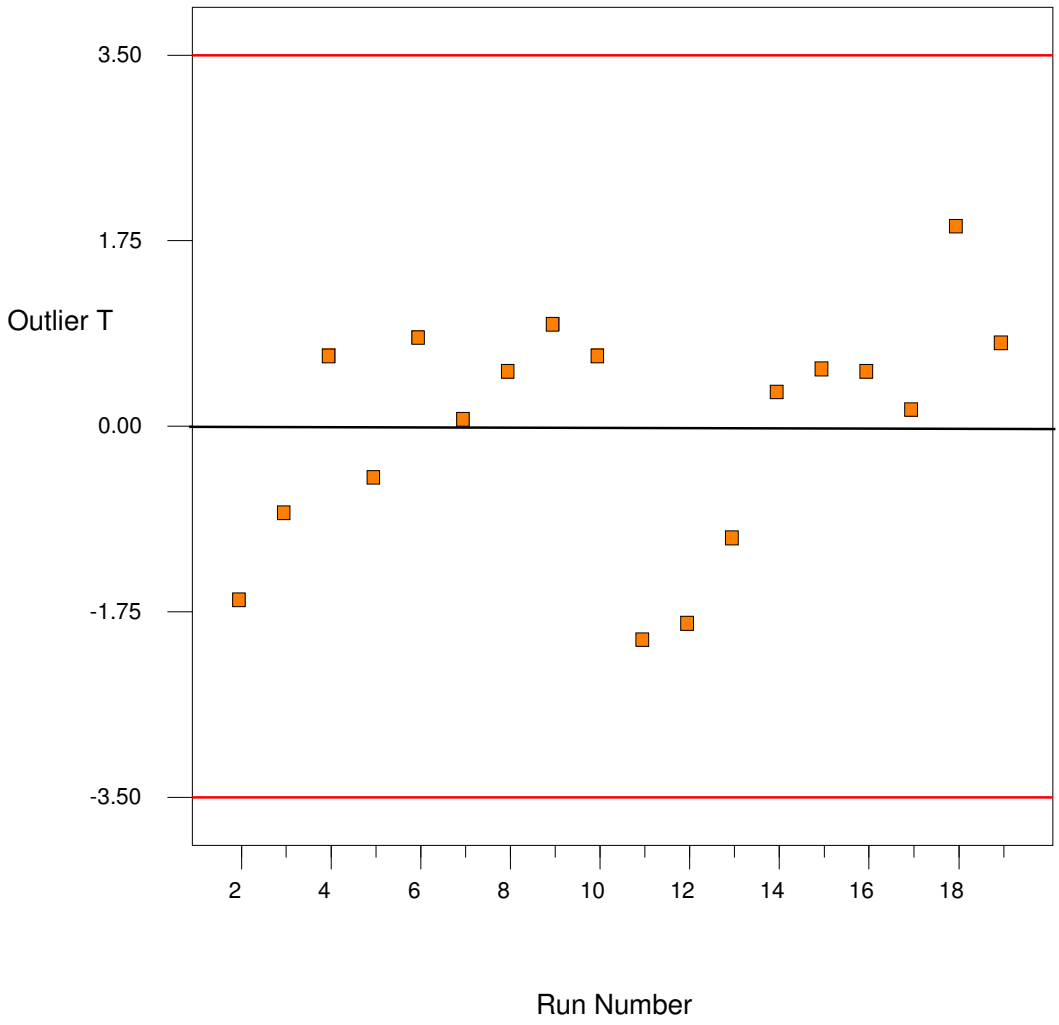

Figure 5: Outlier T plot.

The plots show that the data is normally distributed (Figure 4) and no outliers were detected (Figure 5), which implies that the model fits the data well.

The following tests therefore substantiated the validity of the model:

- Lack of fit test
- Correlation squared
- Test for Normality
- Test for outliers

3.2.6 Confirmation Experiment

A new formulation – where components C and D were excluded - was formulated. It will be referred to as formulations 19 and 20 (duplicate runs). The formulation composition is outlined in Table 28. The concentrations of the other components were not increased to keep the total formulation percentage constant. Instead, the two components were simply excluded from the formulation (refer to Table 28 for modified design).

Table 28: Outline of the components in the verification experiment.

Components (g)					
A	B	C	D	E	F
HPC (100K)	HPC (140K)	PVP-k30	Polyure-Thane-32	PEG-12 Dimethicone	Cetyl dimethicone
1.2	1.2	0	0	0.6	0.6

This formulation is equivalent to formulation 17 and 18 (duplicate) in Table 22, except that PVP and its alternative were excluded without replacement or compensation for the loss of mass.

3.2.6.1 Results

The results from the evaporation studies conducted in the same manner as described in chapter 2 are shown in Table 29.

Table 29: Results from the evaporation studies (in duplicate) conducted over a period of 5 hours for the confirmation experiment.

Time (hr)	**0**	**1**	**2**	**3**	**4**	**5**
Formulation	**Fragrance Concentration (g/L)**					
19	0.341	0.235	0.201	0.125	0.045	0
20	0.374	0.290	0.228	0.142	0.0528	0

Unfortunately, the elimination of components C and D did not extend the period over which the fragrance sample evaporated. The ideal release period for a fixative formulation is over a period of 6 hours or greater. This may however be due to the fact that the initial amount of the fragrance loaded into the sample was already extremely low and the amount of the fragrance component left after 4 hours of incubation is too small to be detected by the GC.

The results from Table 29 were compared directly to those of formulation 17 and 18 (see Tables 22 and 23), from which the modified formulation was derived.

An exponential model was fitted to the data in Table 29, but it was established that it does not provide the best fit. A linear model was however more appropriate. This implies that the results from the modified formulation are focussed on the linear part of the exponential model. It does not imply that the exponential model is incorrect, but simply that the data represents the linear part thereof.

3.2.6.2 Analysis of duplicate runs (formulations 19 & 20).

Before comparing formulations 19 and 20 (duplicate runs) to the formulations where components C and D are present (formulations 17 and 18), it had to be established whether the duplicate runs (formulations 19 and 20 in Table 29) are equal to one another. Dummy regression analysis was carried out, where D = 0 for formulation 19 and D = 1 for formulation 20. It was concluded that there is no significant difference between the rate constants of the duplicate data sets (formulations 19 and 20; $p = 0.387$). The same principle of comparing the modified and original formulation rate constants to one another in the next section 3.2.6.3, was applied here (in section 3.2.6.2). Formulations 17 and 18 (duplicate runs) were also compared to one another in a similar fashion and it was found that there is no significant difference between the two datasets ($p=0.97$).

3.2.6.3 Formulations 17 &18 vs. formulations 19 & 20.

Dummy regression analysis was used to compare the evaporation results of formulations 17 and 18 to that of formulations 19 and 20 (i.e the duplicate runs where factors C and D were omitted).

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Table 30*:* Dummy regression analysis design.

Formulation	Time (hours)	D	Time-D	C_a (g/L)
19 (C & D omitted)	0	0	0	0.341
	1	0	0	0.235
	2	0	0	0.201
	3	0	0	0.125
	4	0	0	0.045
	5	0	0	0
20 (C & D omitted)	0	0	0	0.374
	1	0	0	0.290
	2	0	0	0.228
	3	0	0	0.142
	4	0	0	0.053
	5	0	0	0
17 (C & D present)	0	1	0	0.376
	1	1	1	0.255
	2	1	2	0.113
	3	1	3	0.088
	4	1	4	0
	5	1	5	0
18 (C & D present)	0	1	0	0.362
	1	1	1	0.243
	2	1	2	0.163
	3	1	3	0.048
	4	1	4	0
	5	1	5	0

The model is:

$$\hat{C}_a = b_0 + b_1*\text{Time} + b_2*D + b_3*D*\text{Time} \qquad \text{(Eqn. 3.6)}$$

Where (also applicable to Table 30):

D : Binary dummy variable;

$\hat{C}_a$: Predicted response, which is the concentration of the fragrance after specified incubation period (time);

b_x : Coefficients associated with factors.

For formulations 19 and 20, where PVP and polyurethane-32 were omitted, D = 0.

The equation simplifies to:

$\hat{C}_a = b_0 + b_1*Time + b_2*(0) + b_3*(0)*Time;$

This is equal to:

$\hat{C}_a = b_0 + b_1*Time$ (Eqn. 3.7)

For formulations 17 and 18, where the PVP-components (C-D) were present, D = 1.

Substituting this D value into the original equation (eqn. 3.6) the following equation is obtained:

$\hat{C}_a = b_0 + b_1*Time + b_2*(1) + b_3*(1)*Time;$

This simplifies to:

$\hat{C}_a = b_0 + b_1*Time + b_2 + b_3*Time$

Thus: $\hat{C}_a = (b_0+b_2) + (b_1+\mathbf{b_3})Time$ (Eqn. 3.8)

For the polyvinylpyrrolidone containing formulations (formulations 17 and 18) to differ from formulations 19 and 20 (where components C and D were omitted), a significant difference in the concentration gradients of the two formulations is required. For this to occur, β_3 should **not** be equal to zero (reject null hypothesis which states that $\beta_3 = 0$ when $p < 0.05$) – this will prove that the gradient of the polyvinylpyrrolidone-free formulation (19 and 20) differs significantly from formulations 17 and 18 (when $\beta_3 = 0$, then the gradient from equation 3.8 simplifies to that of equation 3.7). Note that b represents the estimated coefficient (sample dependent and β the true coefficient.

Formulations 17 and 18 (to which exponential models were fitted, see Figures O and P, Appendix B), were compared to the duplicate modified formulations (formulations 19 and 20) using dummy regression analysis (described above). Here D = 0 for formulations 19 and 20; and D = 1 for formulations 17 and 18. To facilitate in the comparison between rate constants of the linear and exponential models fitted to the respective data sets, log-transformation had to be applied. Further, to prevent taking logs from a zero value, 0.1 was

added to all of the Y-values (concentrations (g/L)). It was proven that there is a statistically significant difference between formulations 17 and 18 (duplicate runs), relative to formulations 19 and 20 (duplicate runs) which produced a more favourable (less negative) rate of fragrance loss ($\beta_3 = 0$; p=0.0002). The elimination of components C and D from the formulation composition, as suggested in section 3.2.5.5 does in fact improve the "slow release" properties of the fixative formulation.

3.2.7 Comparison with the original formulation (2009)

To establish whether the formulations in this study, using the alternative ingredients, do in fact perform better than the formulation from the B Sc Honours project in 2009, Appendix A), the rate of fragrance loss of this original, 2009 formulation was compared to some of the modified formulations in Table 22, the results of which are shown in Table 23. Formulation 3 (most favourable rate constant from Table 25) and formulation 6 (least favourable rate constant form Table 25) were selected (see Table 31 for raw data). The comparison of these formulations with the 2009 formulation is shown in Figure 6.

Table 31: Results from original formulation.

	Time (hrs)					
Formulation	**0**	**1**	**2**	**3**	**4**	**5**
Original 1	0.329	0.255	0.191	0.110	0.064	0
Original 2	0.389	0.266	0.211	0.088	0	0
3	0.425	0.307	0.19	0.149	0	0
6	0.519	0.199	0.141	0.074	0	0

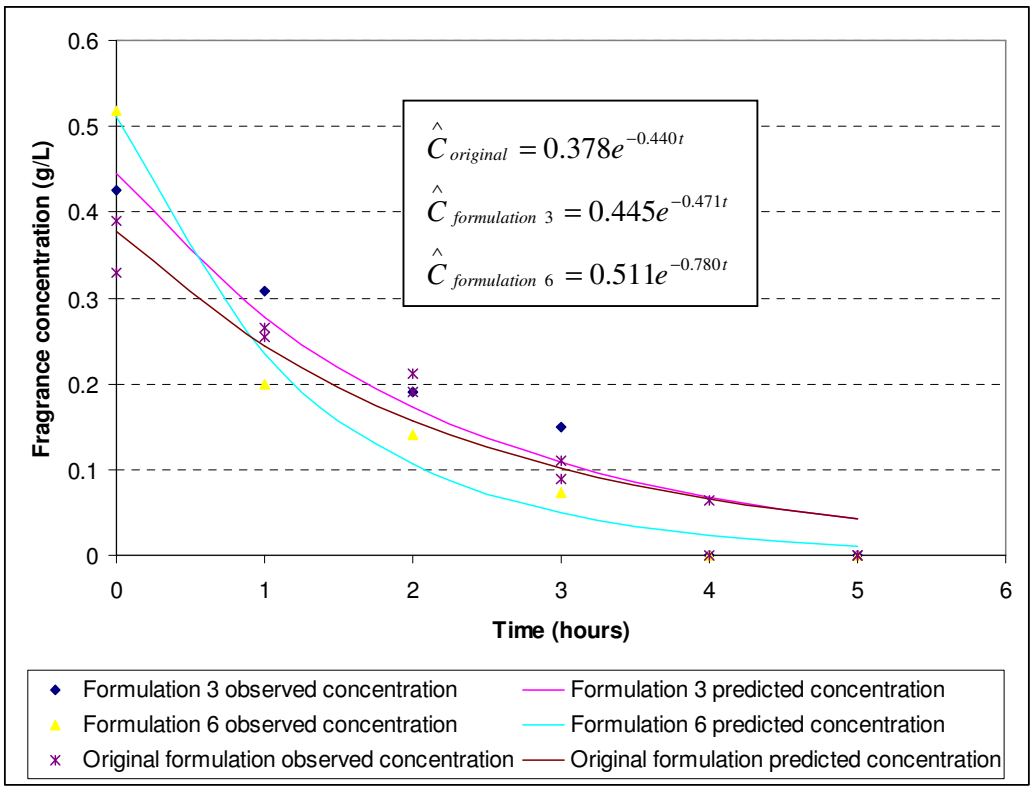

Figure 6: 2009 formulations vs. modified formulations (3 and 6).

3.2.7.1 Comparison of duplicate runs of the 2009 formulation

The original (2009) formulation was tested in duplicate (1 and 2), and both datasets are included in Figure 6 above. A paired t-test was performed on the duplicate dataset (evaporation results) to determine whether they are equal to one another, and it was established that there is no significant difference between them (null hypothesis is accepted: original formulation 1 = original formulation 2; p=0.95).

3.2.7.2 Comparison of formulations 3 and 6 (this study)

To establish whether there is a significant difference between the evaporation rates of formulations 3 and 6 (lowest and highest rate constants respectively, refer to Table 25), dummy regression analysis (the same principle as applied in section 3.2.6) was performed on the evaporation results for these formulations (refer to Table 23). For formulation 3, D = 0 and for formulation

6, D = 1. It was found that there is no significant difference between the evaporation results of formulations 3 and 6 (p = 0.12).

3.2.7.3 Comparison of the 2009 formulation and formulation 3

The evaporation results of the 2009 formulation were compared to the evaporation results of formulation 3 (lowest rate constant and most favourable evaporation results), once again using dummy regression analysis (same principle as applied in section 3.2.6). For the original formulation, D = 1 and for formulation 3, D = 0. It was found that there is no significant difference between the evaporation results (rate constants) from the original formulation relative to formulation 3 (p = 0.69). This implies that differences in the formulation compositions did not improve nor worsen the efficacy of the fixative formulation in terms of its “slow release” properties.

3.2.7.4 Suggested future work

For possible future work, the rate constant for the decrease of the fragrance concentration to 5% of its initial value in 8 hours was calculated on the basis of the data from this dissertation using equations 3.1 and 3.3. This proposed rate constant is -0.374 g/L per hour, which is associated with a half life of 1.85 hours. This proposed rate constant may be used in future as a references point to aid in the possible optimization of this fixative formulation.

CHAPTER 4

SUMMARY AND CONCLUSIONS

Curves were successfully fitted to the evaporation results of the 18 formulations and the rate constant for each formulation determined. It was established that formulation 3 produces the most favourable evaporation results (k = -0.47 g/L per hour; $t_{1/2}$ = 1.47 hours) and formulation 6 the least desirable evaporation results (k = -0.78 g/L per hour; $t_{1/2}$ = 0.89 hours) Visually it seemed as if the evaporation results of the two most extreme formulations differ significantly from one another, but the contrary was proven when the evaporation results (rate of fragrance loss over time) were compared using dummy regression analysis (p = 0.12).

Statistical modelling (validated) and general least squares regression analysis were used to establish which of the 6 components (Table 22) results in the observed variation in the 'rate constant' of the fragrance within various fixative formulations (the statistical software package, Design Expert version 5.0.9[b] was used). All non-significant coefficients ($p \geq 0.05$) from the least square regression were eliminated using backward regression. Only statistically significant terms remained ($p \leq 0.05$). The following final response surface model for the evaporation rate constants was obtained:

$$k = b_0 + b_1X + b_3Z + b_6XZ \qquad \text{(Eqn.3.5)}$$

where X represents components A and B; and Z represents components E and F.

The values of the coefficient estimates (b_i) are tabulated in Table 27. Components (A to F) were interpreted individually, keeping the other components constant. It was concluded that by increasing the concentrations of components X (HPC 100K and HPC 140K) and components Z (SF1288 and cetyl dimethicone) respectively, the "slow release" properties of the

fragrance incorporated into the various fixative formulations was improved (b_1 = +0.25, p = 0.0002; b_3 = +0.36, p = 0.0007). The interaction between X and Z (A-B with E-F), has the opposite effect to components X and Z (as individual components) weakening the "slow release" properties of the fixative formulations (b_6 = -0.39, p <0.0001). This effect is, however, not as pronounced as the positive effect from components X (A-B) and Z (E-F). Components C and D do not appear to improve nor weaken the "slow release" properties of the fixative formulations. Components C and D (PVP-K30 and polyurethane-32 respectively) were excluded from a formulation where all of the components were present in their centre-point concentrations (formulation 17 and 18). This was executed without changing the composition of the other components (total mass 37.6 g). Using dummy regression analysis, the evaporation results from formulations 17 and 18 (duplicate runs) were compared to formulations 19 and 20 (where components C and D were omitted) and it was found that the exclusion of components C and D from formulations 17 and 18 does in fact improve the "slow release" properties of the fixative formulation, supporting the conclusions made in section 3.2.5.5.

It is suspected that the filming properties (brittleness) of this polymer group, polyvinylpyrrolidone[19], may have contributed to the observed results where the exclusion of the particular ingredient (group of ingredients in this case) resulted in more desirable "slow release" results.

The original (2009) formulation (Appendix A) was compared to formulation 3 (most favourable evaporation results and rate constant) using dummy regression analysis and it was found that there is no significant difference between evaporation results of the 2009 and the formulation 3 in this study (p = 0.69). This implies modification of the 2009 formulation through the addition of alternative ingredients did not improve nor weaken the "slow release" properties of the original, 2009 formulation.

4.1 Approval of research hypothesis

The research hypothesis for this study stated that the slow release effectiveness of a typical perfume fixative can be improved by the careful replacement of fixative components in a designed experiment using the rate of active disappearance from a glass surface as a measure of effectiveness.

The research hypothesis was accepted, since the slow release effectiveness of a typical perfume fixative was improved by the careful replacement and elimination of some fixative components in a designed experiment using the rate of active disappearance from a glass surface. Evidence suggested that the removal of the component polyvinylpyrrolidone (C) and its alternative, polyurethane-32 (D) (components C and D forms a group and is referred to as Y) would improve the effectiveness of the fixative formulation in terms of its "slow release" properties. Confirmation experiments were conducted, and verified these results.

The answers gained from this study to address the original aims/objectives set for the study are as follows:

1. **To investigate whether certain ingredients in the original perfume fixative formulation can be replaced by alternative, yet similarly acting components.**

   Certain ingredients in the original fixative formulation were successfully replaced by alternative ingredients without any significant change in the "slow release" properties.

2. **To investigate whether the effectiveness of "slow release" in the presence of a perfume fixative formulation can be measured effectively by the rate of evaporation of an "active" substance from a glass surface under controlled conditions.**

   The method was validated by conducting a study in triplicate and comparing the resultant gradients and intercepts of the three independent runs to one another (dummy regression analysis). It was established that

there is no significant difference between the gradients and intercepts of the triplicate runs (section 2.2.6).

3. To investigate whether the rate of evaporation can be used as an effective measure of "slow release".

The rate of evaporation can be used as an effective measure of "slow release", but not solely in terms of the rate of evaporation (rate constant) of the fragrance relative to each fixative formulation. Dummy regression analysis (for example) should be implemented to compare the evaporation results to establish whether a difference in rate constants is indicative of a TRUE difference in the evaporation rate of the fragrance from the fixative formulations or whether the differences observed are purely due to experimental error.

4. To investigate whether certain individual components can improve or worsen the effectiveness of the fixative formulation and can be identified in a designed experiment.

In this designed experiment, groups of components rather than individual components could be identified. This is because the sum of the components (original ingredient and its alternative) in each group is constant. They are therefore considered as a single entity, for example, HPC (100K) and its alternative (140K) are considered as one. The results were discussed earlier in this section. In summary: Increasing the concentration of components A-B (HPC 100K and HPC 140K) and E-F (PEG-12 Dimethicone and cetyl dimethicone) improves the 'slow release' properties of the fixative formulations and the interaction between the HPC and silicone groups has the opposite effect, but not as pronounced as the positive effects from A-B (HPC 100 and 140K) and E-F (the silicones). Components C-D (PVP-K30 and polyurethane-32) were not part of the final model (p-values associated with the coefficients, b_3 and b_4, were >0.05 and these coefficients were thus rejected). Increasing the concentrations of components C-D is not expected to improve the evaporation rate of the fragrance. A confirmatory experiment was

conducted and it was established that the exclusion of these two components does, in fact, decrease the rate of fragrance evaporation.

4.2 Recommendations

It is suggested that a more intricate experimental design, where the components and their alternatives are independent of one another, should be considered. Future formulations should investigate the effects of the components polyvinylpyrrolidone and polyurethane-32 relative to the effectiveness of the fixative formulations to establish whether one of these components or both of them are responsible for the observed effects (as confirmed in this dissertation). A higher initial concentration, for the purposes of the evaporation study, should be considered (within the limits of the allowed or recommended levels of the selected active component). An experimental design should also be considered where the concentrations of groups of correlated components do not add up to a fixed mass, but within a selected mass range instead.

Further recommendations:
This study focused on the “slow release” properties of the formulation, but future studies should consider other factors which may influence this property when such a fixative formulation is incorporated into a usable product (i.e. a perfume, cream, hair product or any other cosmetic product).

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Software programs used:

a Statistica® Version 6.0, produced by StatSoft. Inc.

b Design-Expert® Software, Version 5.0, produced by Stat-Ease Inc.

c Microsoft® Office Excel 2003.

APPENDIX A

Table A: Original Formulation.

Slow release formulation

Phase	Ingredient	mass %
A	JR30/water	13.6
	SF1288	3.4
B	HPC (Hydroxypropyl cellulose)	6.8
	PVP-K30	6.8
	CDE (coconut oil)	1.4
	PG (propylene glycol)	68.0
	Total:	**100**

Method (100g total)

Phase A

Prepare a 2 % solution of polyquaterium-10 in distilled water at RT and stir until clear (~75 minutes) using a magnetic stirrer bar.

To 13.6g of the clear JR30/water mixture add 3.4g of SF1288 while stirring (using a magnetic stirrer bar).

Phase B

Dissolve 6.8g of HPC in 68g propylene glycol and homogenise while heating the Solution in a water bath until it becomes clear.

Add 6.8g PVP and homogenise while heating the solution in a water bath until Clear.

Add 1.4g CDE to the PVP/HPC mixture and homogenise.

Add phase B (higher volume phase) to phase A (lower volume phase) and homogenise (water in oil emulsion). Final product is a clear, stiff gel.

APPENDIX B

Figures A to P - Curve fitting formulations 3-18

For all of the curves (figures A-P), the concentration on the y-axis refers to the fragrance concentration. Also note that all of the concentrations, as indicated in the equations within the figures, are the predicted fragrance concentrations (Ĉ).

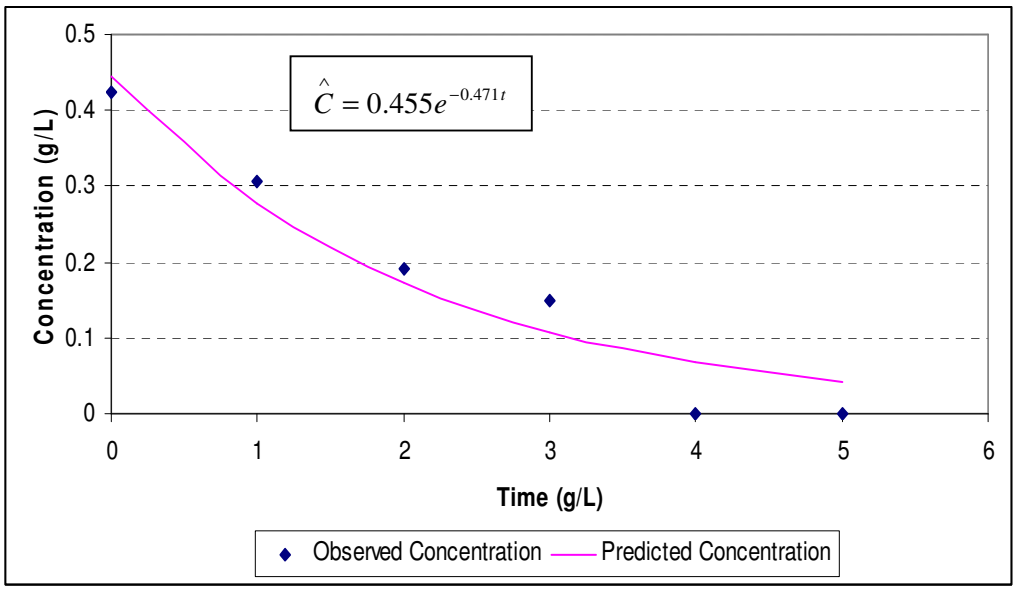

Figure A: Results of curve fitting for formulation 3.

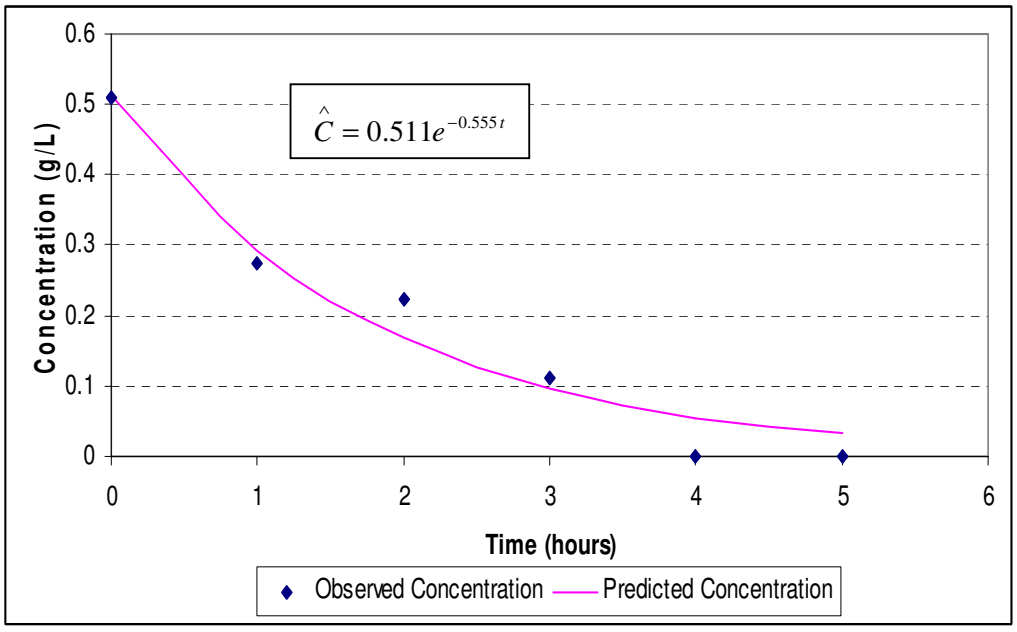

Figure B: Results of curve fitting for formulation 4.

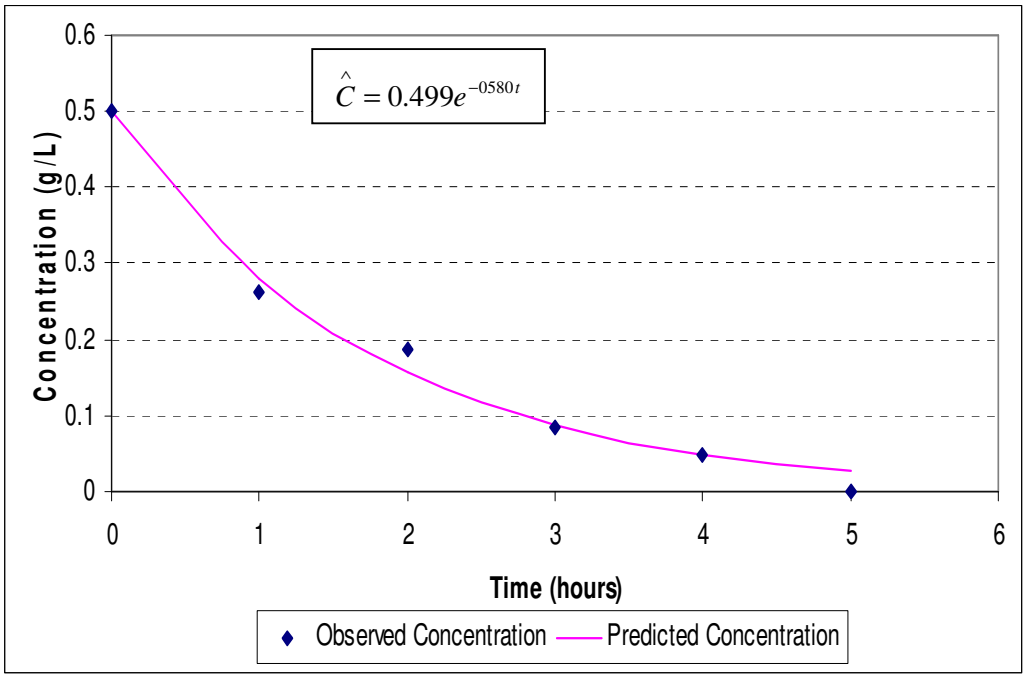

Figure C: Results of curve fitting for formulation 5.

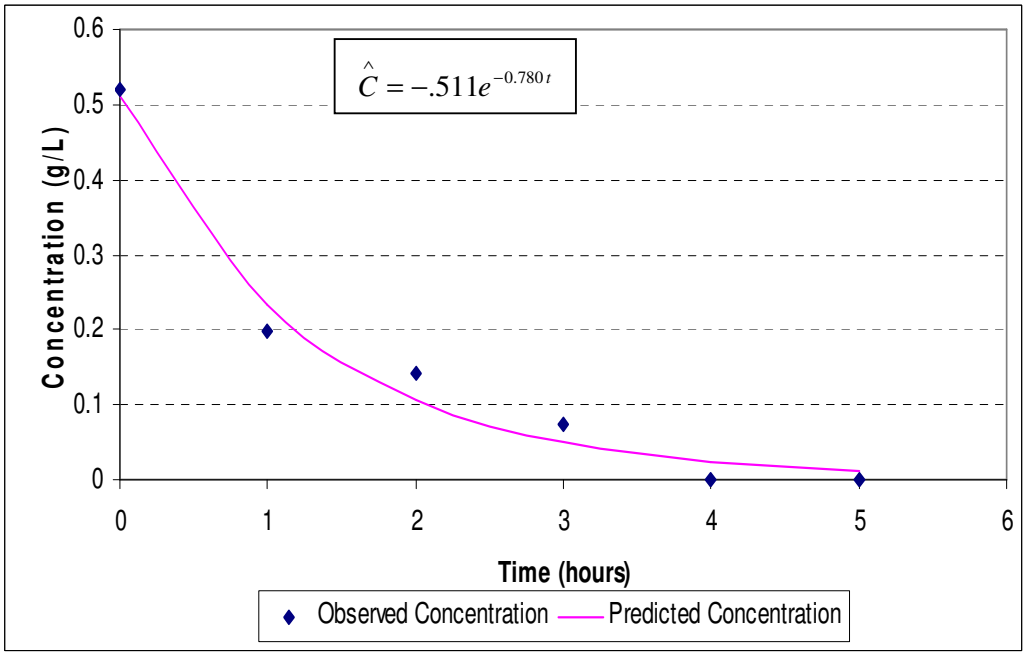

Figure D: Results of curve fitting for formulation 6.

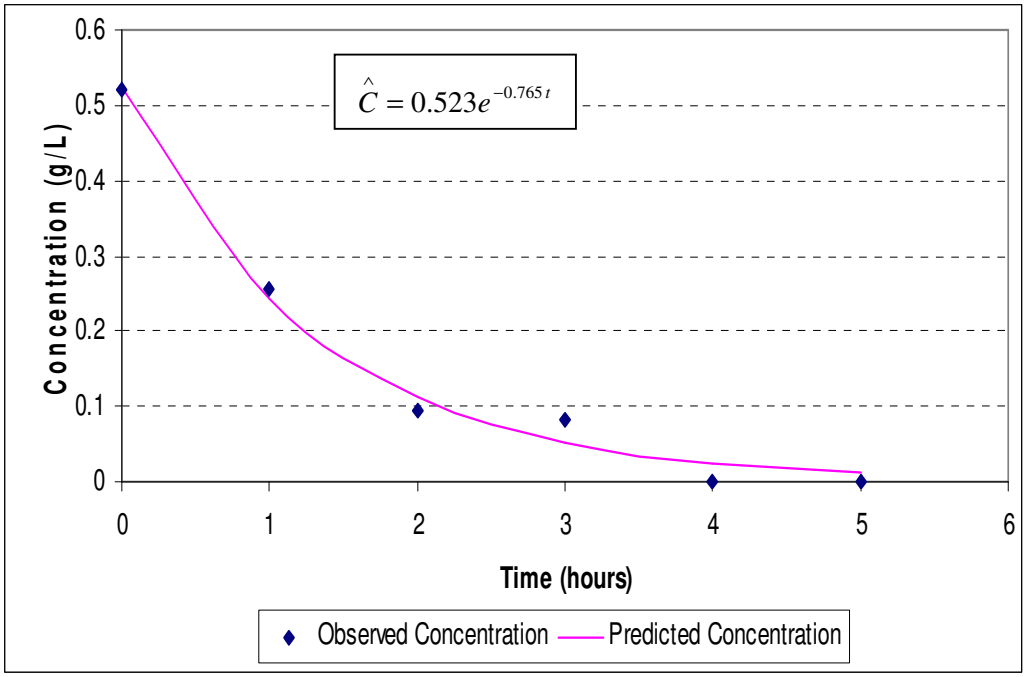

Figure E: Results of curve fitting for formulation 7.

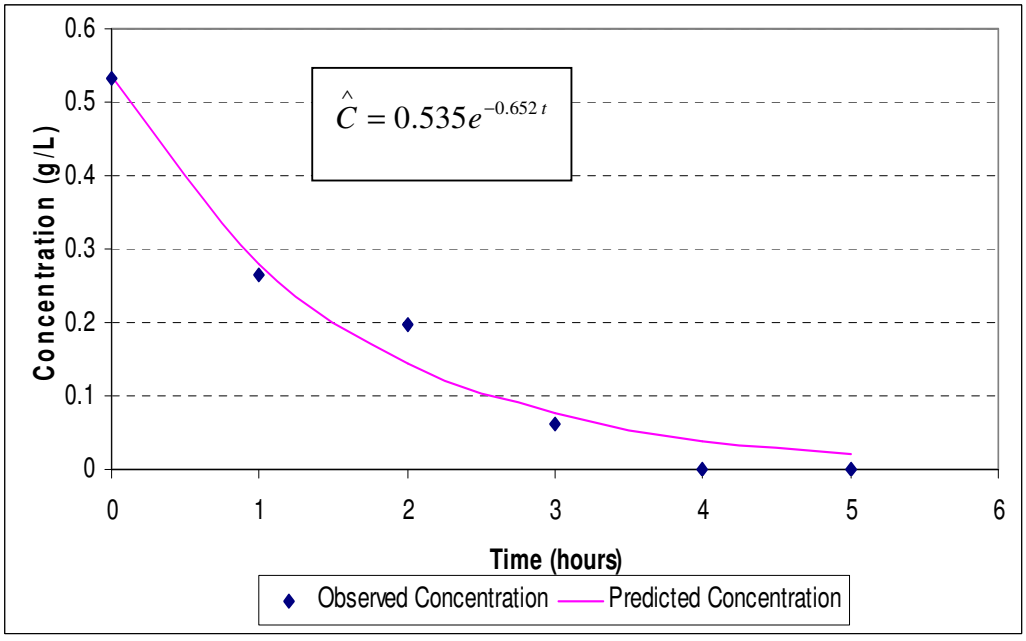

Figure F: Results of curve fitting for formulation 8.

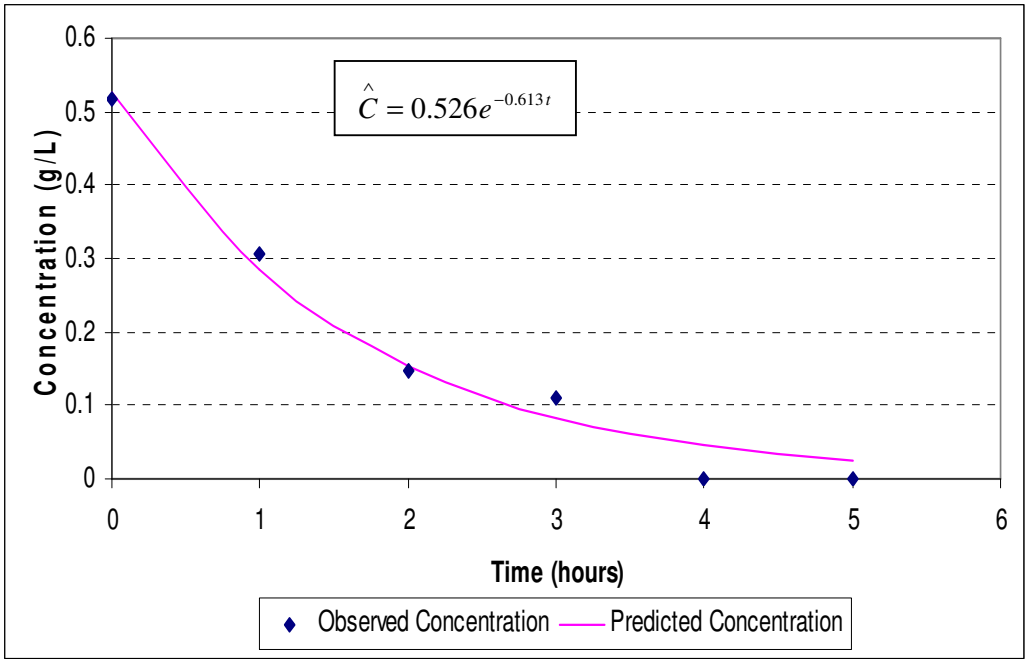

Figure G: Results of curve fitting for formulation 9.

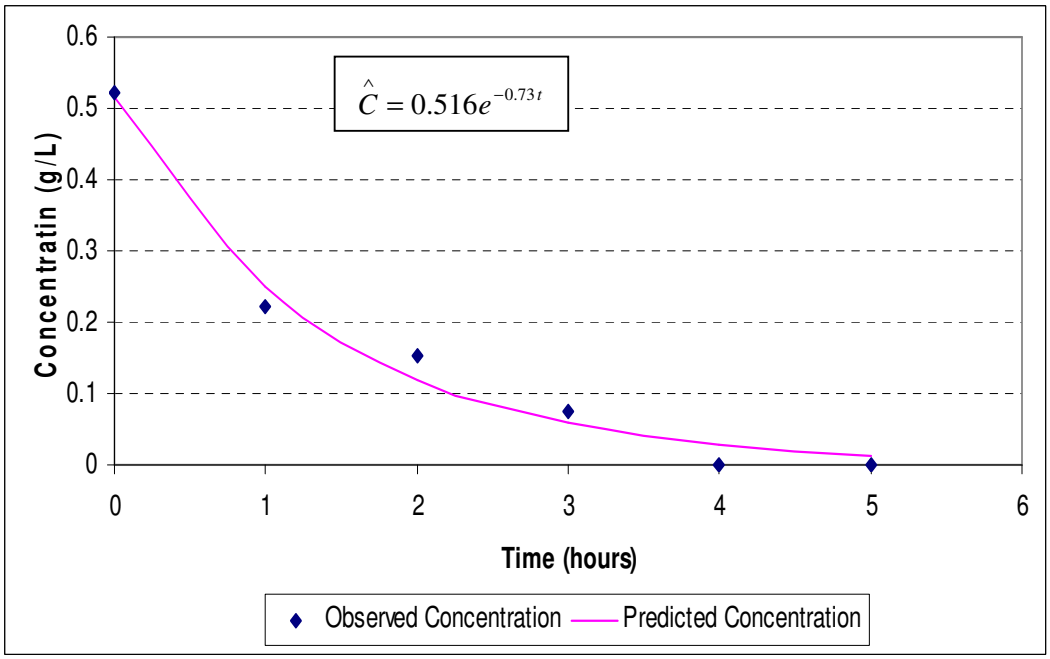

Figure H: Results of curve fitting for formulation 10.

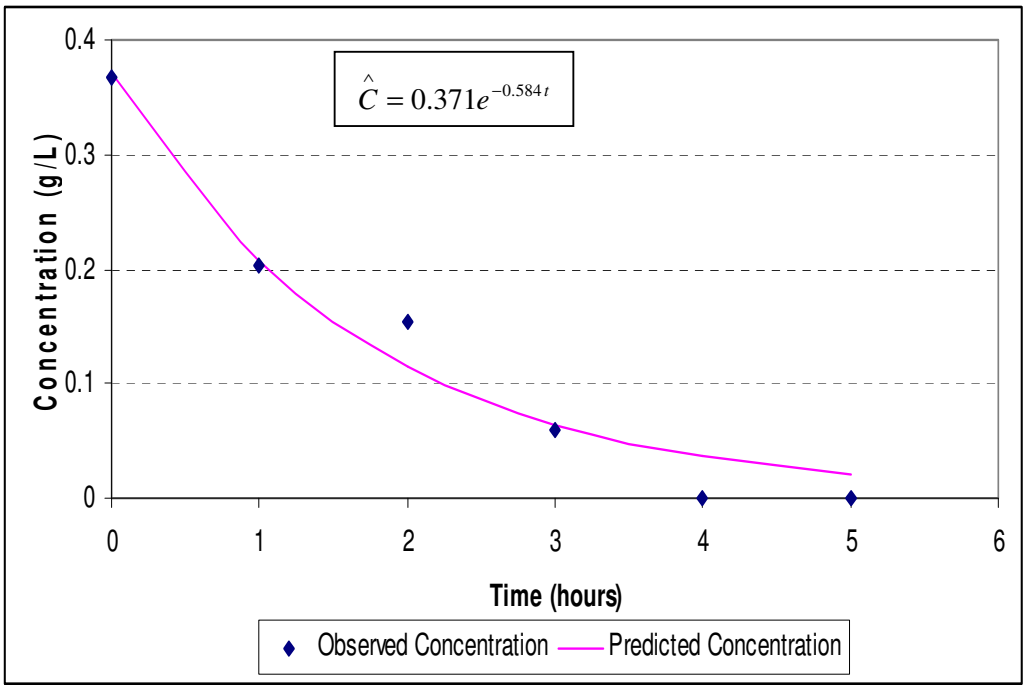

Figure I: Results of curve fitting for formulation 11.

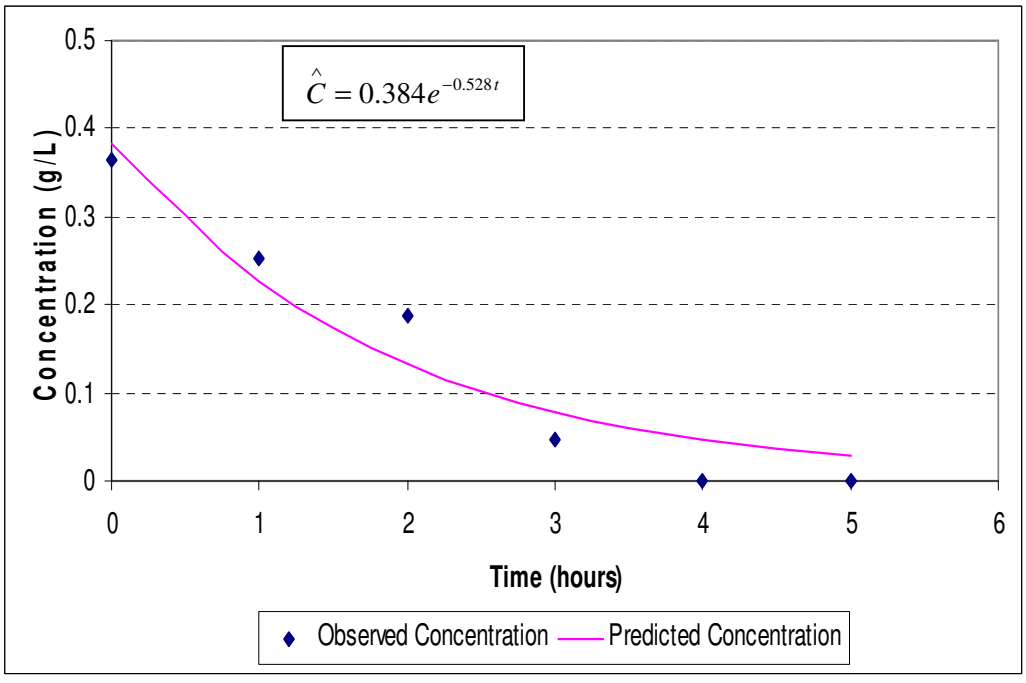

Figure J: Results of curve fitting for formulation 12.

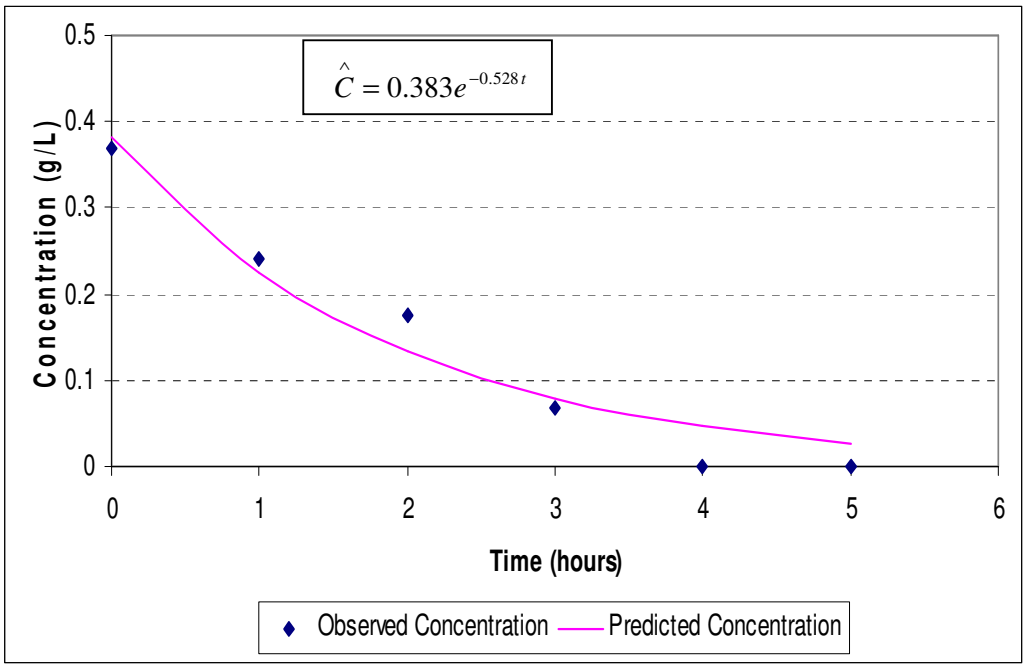

Figure K: Results of curve fitting for formulation 13.

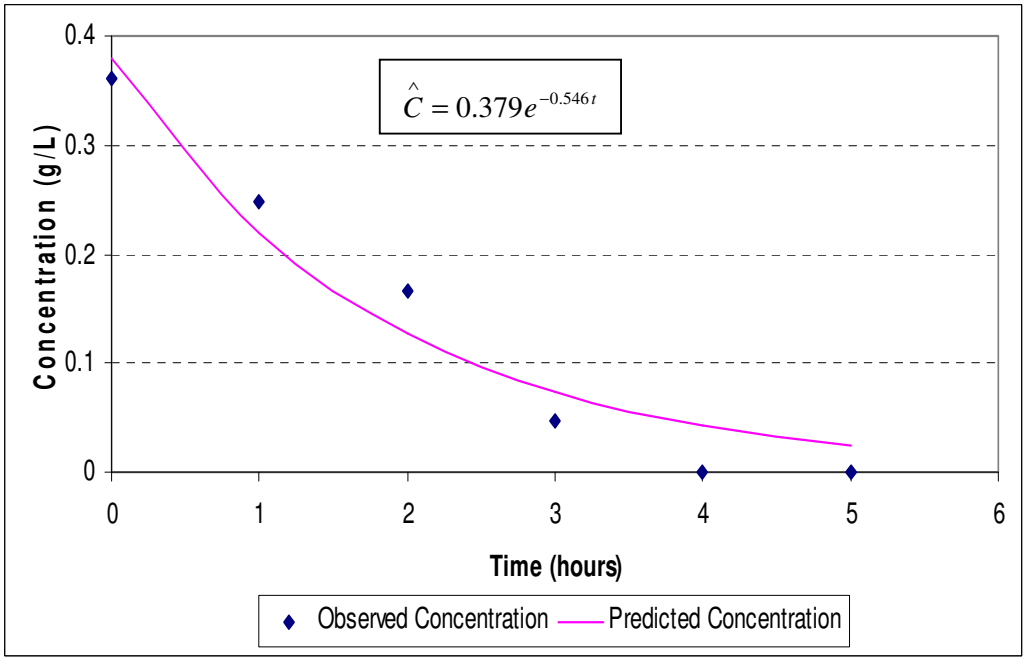

Figure L: Results of curve fitting for formulation 14.

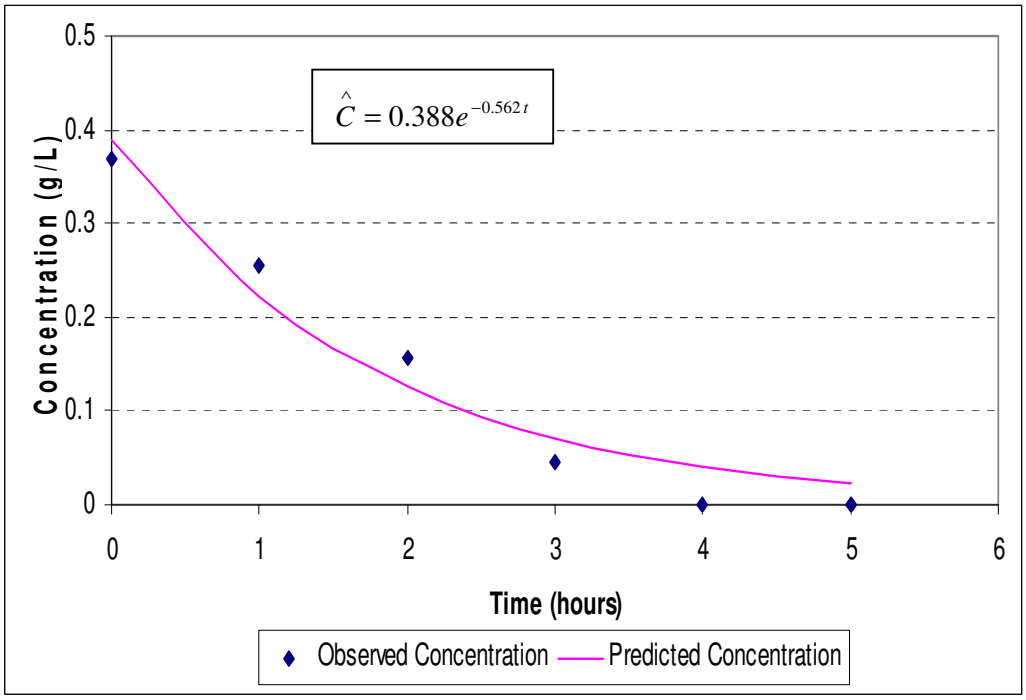

Figure M: Results of curve fitting for formulation 15.

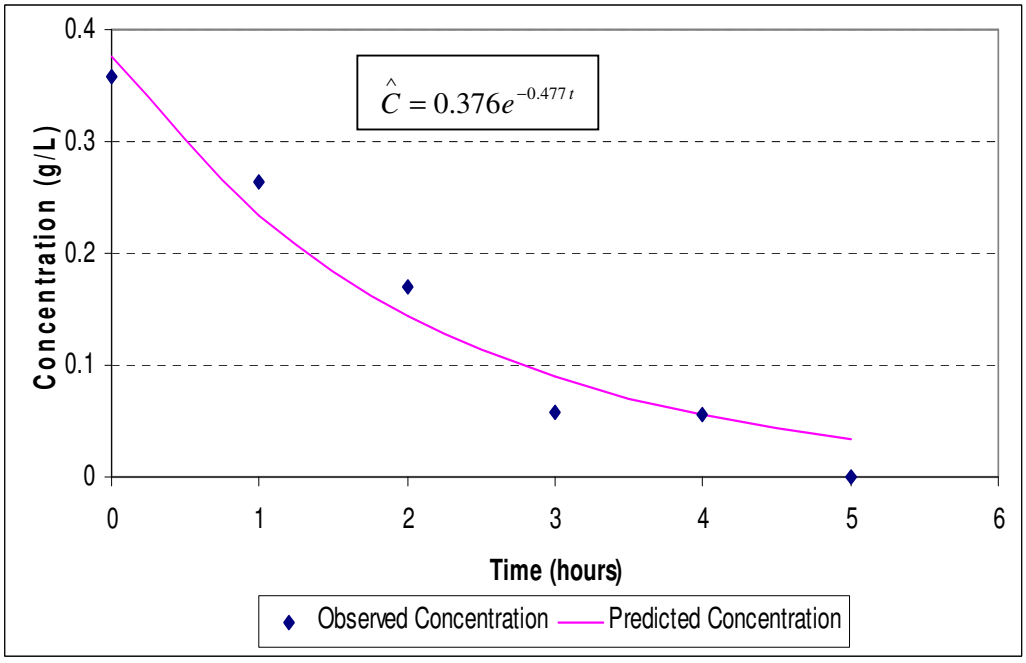

Figure N: Results of curve fitting for formulation 16.

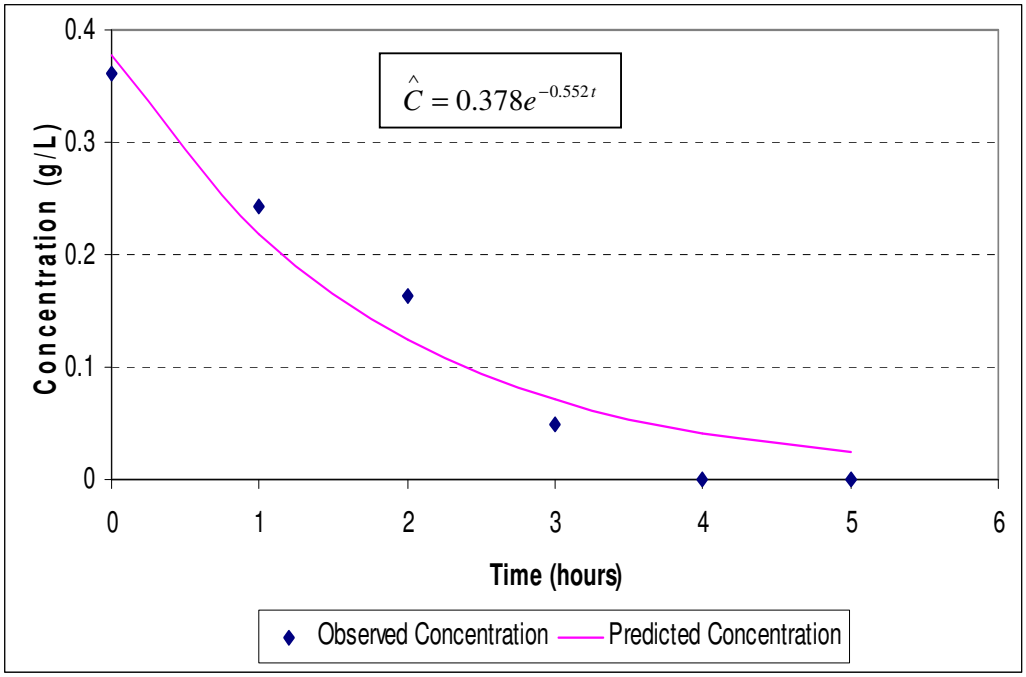

Figure 0: Results of curve fitting for formulation 17.

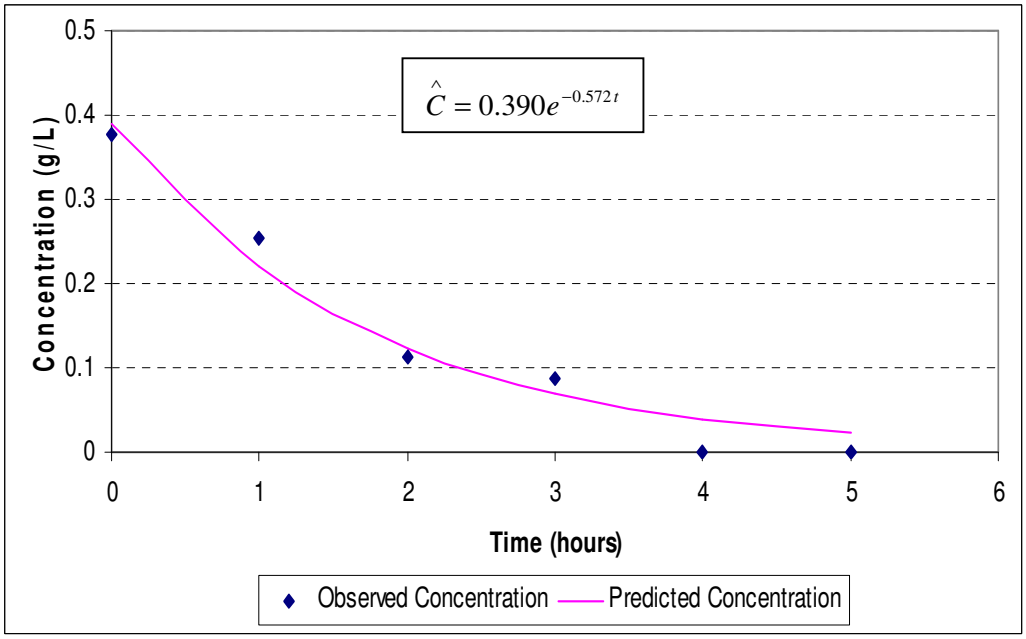

Figure P: Results of curve fitting for formulation 18.

APPENDIX C

Table B: Summary of design, evaporation results and responses.

	Ingredients (grams)							0	1	2	3	4	5	Response	
Formulation	**HPC (100K)**	**HPC (140K)**	**PVP**	**Polyurethane-32**	**PEG-12 Dimethicone**	**Cetyl dimethicone**	**Total**	**Fragrance concentration (g/L)**						**Rate constant (k)**	**Half life (hours)**
1	0.4	2	1.2	1.2	0.2	1	6	0.466	0.221	0.144	0.057	0.055	0	0.65	1.06
2	0.4	2	0.4	2	0.6	0.6	6	0.431	0.236	0.16	0	0	0	0.68	1.01
3	0.4	2	2	0.4	1	0.2	6	0.425	0.307	0.19	0.149	0	0	0.47	1.47
4	1.2	1.2	2	0.4	0.2	1	6	0.509	0.276	0.223	0.111	0	0	0.56	1.25
5	0.4	2	0.4	2	1	0.2	6	0.501	0.263	0.187	0.083	0.047	0	0.58	1.19
6	2	0.4	0.4	2	1	0.2	6	0.519	0.199	0.141	0.074	0	0	0.78	0.89
7	2	0.4	2	0.4	1	0.2	6	0.52	0.254	0.095	0.081	0	0	0.77	0.91
8	0.4	2	0.4	2	0.2	1	6	0.533	0.265	0.198	0.062	0	0	0.65	1.06
9	1.2	1.2	0.4	2	0.2	1	6	0.517	0.306	0.148	0.112	0	0	0.61	1.13
10	2	0.4	0.4	2	1	0.2	6	0.522	0.221	0.153	0.076	0	0	0.73	0.95
11	0	2.4	2.4	0	0.6	0.6	6	0.367	0.202	0.155	0.06	0	0	0.58	1.19
12	2.4	0	2.4	0	0.6	0.6	6	0.365	0.252	0.187	0.046	0	0	0.53	1.31
13	2.4	0	0	2.4	0.6	0.6	6	0.369	0.241	0.177	0.067	0	0	0.53	1.31
14	0	2.4	0	2.4	0.6	0.6	6	0.361	0.248	0.166	0.047	0	0	0.55	1.27
15	1.2	1.2	1.2	1.2	1.2	0	6	0.37	0.256	0.156	0.045	0	0	0.56	1.23
16	1.2	1.2	1.2	1.2	0	1.2	6	0.358	0.264	0.17	0.058	0.056	0	0.48	1.45
17	1.2	1.2	1.2	1.2	0.6	0.6	6	0.362	0.243	0.163	0.048	0	0	0.55	1.25
18	1.2	1.2	1.2	1.2	0.6	0.6	6	0.376	0.255	0.113	0.088	0	0	0.57	1.21