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Quantitative Determination of Multiple Ingredients in Topical Formulation by Gas Chromatography (GC)

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PURPOSE

Gas Chromatography (GC) is a typical chromatographic method used to separate and quantitatively determine analytes that can be volatized without decomposition. Many excipients widely used in topical semi-solid and liquid formulations, as solvents, penetration enhancer, humectant, surfactant, thickener and preservative, can be quantitatively tested by GC. Examples of such excipients are listed in Table 1. In order to quantitatively determine these multiple excipients, in a given formulation, a suitable GC method that can be applied to separate these excipients and quantitate them, was developed and validated.

METHODS

In this study, the excipients that could be simultaneously quantitatively determined, from a single formulation, were Ethanol, Propylene Glycol (PG), Diethylene Glycol Monoethyl Ether (DGME), Benzyl Alcohol (BA), Dimethyl Isosorbide (DMI), Isopropyl Myristate (IPM), Phenoxyethanol, Glycerin, Cetyl Alcohol and Stearyl Alcohol. 1-Propanol and 1-Decanol were used as internal standards, and Methanol was used as solvent. A series of standard solutions with known concentration were prepared for linearity study. Accuracy study was performed by spiking known amount of these excipients into a placebo cream formulation at 50%, 100% and 150% level of nominal concentration. Following GC conditions were used:

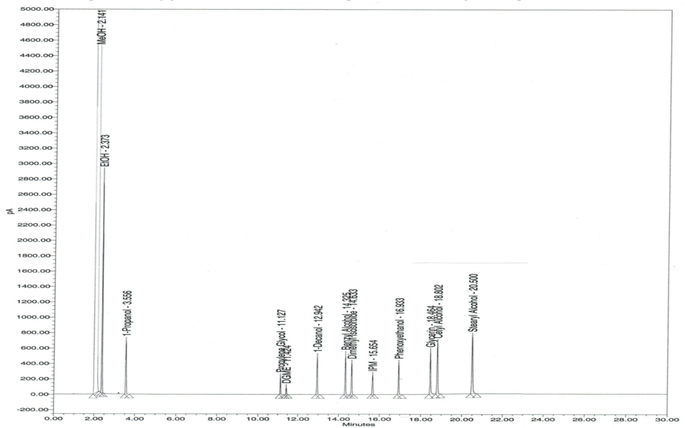
GC System: Agilent 6890 Series
GC Column: ZB-Wax, 1µm film, 30 m x 0.53 mm ID
Detector: FID
Detector Temp: 250ºC
Oven Temp: Initial 50ºC, hold for 2 min; 10ºC/minute to 230ºC; hold for 10 min, Total 30 min
Injector Temp: 230ºC
Injection volume: 2.0 µL with splitless mode.
Flow rate of Helium: 8 mL/min

A typical chromatogram obtained is illustrated in Figure 1.

Table 1 Typical Ingredients Used in Topical Formulations

Ingredient	Function
Ethanol	Solvent
Diethylene Glycol Monoethyl Ether (DGME)	Penetration Enhancer/Solvent
Dimethyl Isosorbide (DMI)	Solvent
Isopropyl Myristate (IPM)	Penetration Enhancer/Solvent
Benzyl Alcohol (BA)	Preservative
Phenoxyethanol	Preservative
Propylene Glycol (PG)	Humectant/Solvent
Glycerin	Humectant/Solvent
Cetyl Alcohol	Emulsifier/Thickener
Stearyl Alcohol	Emulsifier/Thickener

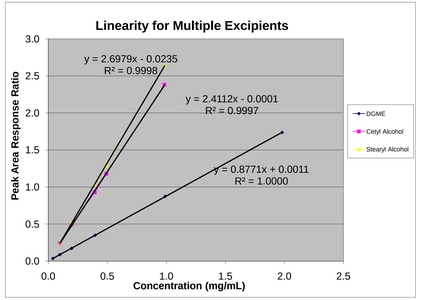
Figure 1 Typical GC Chromatogram of Multiple Ingredients

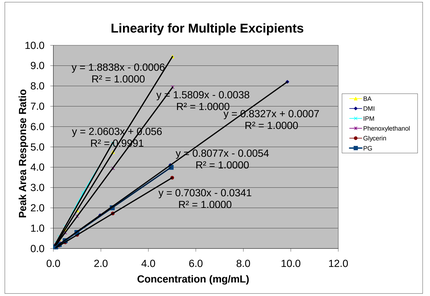


RESULTS

The successful GC method showed that the resolution between Methanol and Ethanol was more than 2.0. A linearity range of 0.9960-49.8016 mg/mL for Ethanol, 0.0992-4.9584 mg/mL for PG, 0.0396-1.9814 mg/mL for DGME, 0.1004-5.0184 mg/mL for BA, 0.1971-9.8536 mg/mL for DMI, 0.0501-2.5066 mg/mL for IPM, 0.1004-5.0220 mg/mL for Phenoxyethanol, 0.1001-5.0040 mg/mL for Glycerin, 0.0984-0.9840 mg/mL for Cetyl Alcohol and 0.0986-0.9860 mg/mL for Stearyl Alcohol with $R^2 \geq 0.999$ has been determined in the method, respectively. % Recovery of Accuracy at 50%, 100% and 150% of nominal concentration for Ethanol, PG, BA, DMI, IPM and Phenoxyethanol in a placebo cream was obtained within range of 98-102% with % RSD (n=3) of less than 2%. All validation parameters met the criteria.

Figure 2 Linearity Curves of Multiple Ingredients





CONCLUSIONS

A suitable GC method has been successfully developed to quantitatively determine multiple pharmaceutical ingredients regularly used in the topical formulations, simultaneously.

FUNDING

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