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Separation and Determination of Phenobarbital and Guaifenesine in Commercial Pharmaceuticals Using Grafted Algerian Bentonite With SE-52 By Gas Chromatography

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Two pharmaceutical compounds *i.e.*, phenobarbital and guaifenesine in several commercial pharmaceutical sources were investigated. These compounds were separated using grafted Algerian bentonite (B_{1100}) with SE-52 as support. The compounds were determined by gas chromatography technique. The obtained analytical results show a good precision and reproducibility with a relative standard deviation of 2.8 and 2.9 % for phenobarbital and guaifenesine, respectively.

Key Words: Algerian bentonite, Phenobarbitall, Guaifenesine, Gas chromatography.

INTRODUCTION

The bentonite is used in diverse industrial domains. It consists of several ores, the aluminium silicate being its main compound[1-4]. Heat and acid treatment of the Algerian bentonite, 'Roussel' quarry near the city of Maghnia, northwest of Algeria, was studied by diverse analytical methods, such as the infrared, X-rays and the differential thermal analysis, the specific surface and the nature of its chemical composition were measured[5]. Chromatographic columns filled with the bentonite material grafted by condensation of silicon SE-52 or silanization with the dimethyl chlorosilane (DMCS) were used for the determination of some normal hydrocarbons compounds mixtures, C_5-C_{12} and C_5-C_{18}, as well as mixtures of some cyclic and aromatic organic compounds[6-8].

In addition to that, the determination of diverse chemical compounds for their conservatives and aromas in pharmaceutical products using Algerian bentonite thermally treated at 650 ºC (B_{650}) followed by silanization with DMCS were carried out[9]. Many reported works[10-24] showed that the phenobarbital and the guaifenesine can be determined by both gas chromatography (GC)[10-18] and by high performance liquid chromatography (HPLC)[19-24].

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The purpose of this paper is to develop gas chromatographic method for the separation and determination of phenobarbital (antiepileptic) and guaifenesine (expectorating) which are involved in the composition of some commercial pharmaceutical products, using grafted Algerian bentonite (B_{1100}) with SE-52 as support.

EXPERIMENTAL

The chromatograms were obtained using a GC-9A gas chromatograph equipped with a flame ionization detector (FID) and chromatopac C-R3A printer (Shimadzu), 1 μL syringe (hamilton) and special reactor for grafting were used. All solvents and chemicals were extra pure grade. Bentonite was obtained from Roussel quarry, near Maghnia town (northwest of Algeria).

Support preparation: A support was prepared from Algerian bentonite, by thermal treatment at 1100 ºC and then treated with 6 N HCl and finally washed by distilled water until the excess Cl^- ions were no longer detectable by the $AgNO_3$ test (B_{1100}). The diameter of granules was in range 125-150 μm. The specific surface area was 12 m^2/g. The support grains into the reaction phial of an oven of grafting by raising the temperature gradually under a weak current of inert pure and dry gas (N_2) were monitored. The temperature was increased gradually until 280 ºC keeping the regularity of nitrogen stream flow during the treatment duration. The device was then left to cool down until the ambient temperature by keeping the stream of nitrogen gas flow running. The obtained support was then introduced into the device of Soxhlet for 48 h using chloroform solvent in order to eliminate the excess of silicone SE-52 without any direct chemical connection to the surface and at the time, the chromatographic of grafted supported material by the silicone SE-52 was obtained.

Preparation of standard solutions of guaifenesine: 1000 mg of guaifenesine dissolved in hydrochloric acid (0.1 N) and then the volume was made to 100 mL using hydrochloric acid solvent. Volumes of 0.5, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 and 12 mL of the previous solution were used to extract guaifenesine with 3 mL of chloroform, in three stages and then the volumes were adjusted with the same solvent to 10 mL. The standard solutions of 5, 10, 20, 30, 40, 50, 60, 70, 80, 90, 100 and 120 mg of guaifenesine in 10 mL solution were prepared.

Preparation of standard solutions of phenobarbital: 1000 mg of phenobarbital dissolved in ethanol and the volume was adjusted to 50 mL. Standard solution of 10, 20, 30, 40, 50, 60, 70, 80, 90, 100, 110 and 120 mg of phenobarbital in 10 mL using ethanol solvent were prepared.

Solutions of samples

Extraction of the guaifenesine: Guaifenesine is extracted from 10 mL pharmaceutical formulations using chloroform in 3 stages and the volume was adjusted to 10 mL.

Extraction of the phenobarbital: Phenobarbital is extracted from a tablet using ethanol in 3 stages and the volume was adjusted to 10 mL.

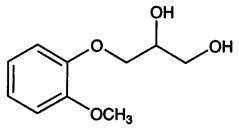
RESULTS AND DISCUSSION

Phenobarbital and guaifenesine were extracted from the following pharmaceutical forms Table-1.

TABLE-1

Pharmaceutical forms	Composition	Produced by
Toplexil (Syrup)	100 mL of syrup contain: 666 mg guaifenesine 33 mg oxomemazine	Saidal, Subsidiary pharmal - Algeria
Toplexil (Syrup)	100 mL of syrup contain: 666 mg guaifenesine 33 mg oxomemazine	Oubari - Syria
Aparoxal (Tablets)	Each tablet contains: 100 mg of phenobarbital	Made by Pierre Fabre medicament Laboratories - France and conditioning by Bio-Galenic, Constantine- Algeria
Dimabarbital (Tablets)	Each tablet contains: 100 mg of phenobarbital	Dimas, Syria
Phenotal-30 (Tablets)	Each tablet contains: 30 mg of phenobarbital	Darou Pakhsh, Iran
Phenotal-60 (Tablets)	Each tablet contains: 60 mg of phenobarbital	Darou Pakhsh, Iran

Determination of guaifenesine: The following conditions were applied for the determination of guaifenesine (**Scheme-I**) using gas chromatography technique.



m.f. = $C_{10}H_{14}O_4$, m.w. = 198.22

Scheme-I: Structure of guaifenesine

Column dimension: 2 mm × 200 cm; Support: Algerian bentonite, mesh: 125-150 μm, specific surface 12 m^2/g and grafted with silicone SE-52; Oven temperature: 230 ºC; Gas vector flow: 40 mL/min (N_2 pure); Injection temperature: 270 °C.

In order to determine guaifenesine in all samples and standards, gas chromatography column was packed with grafted Algerian bentonite (B_{1100}) with SE-52 as a support. The separation of extracted guaifenesine was completely isolated with high sensitivity. The retention time of guaifenesine was 2.95 min. A calibration curve was constructed by the standard procedure. Good linearity ($S = 9663.3x + 892.5$, $R^2 = 0.9991$; x = m, mg (guaifenesine)/10 mL and y = S, area of peak) was obtained within the range 10-120 mg (guaifenesine)/10 mL (Fig. 1). All the pharmaceutical separated formulations results of the guaifenesine are summarized in Table-2. Finally, the injected quantity for both standard solutions and samples was 0.4 μL.

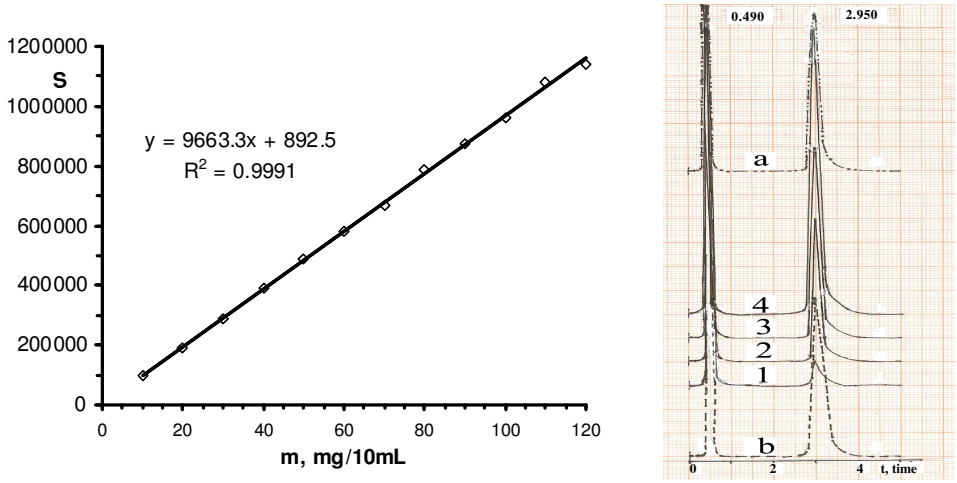


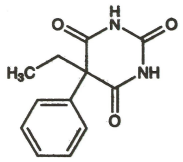
Fig. 1. Determination and separation of guaifenesine using Algerian bentonite (B_{1100}) grafted with silicone SE-52 as support in gas chromatography: (1-4) standard 10, 60, 80 and 120 mg/10 mL; (sample a) - Toplexil (Syrup - Saidal, subsidiary Pharmal - Algeria); (sample b) - Toplexil (Syrup - Oubari, Syria). (Column 200 cm × 2 mm, temperature 230 ºC, N_2 flow 40 mL/min, inject temperature 270 ºC, V= 0.4 µL)

TABLE-2
DETERMINATION OF GUAIFENESINE IN PHARMACEUTICALS USING ALGERIAN BENTONITE (B_{1100}) GRAFTED WITH SE-52 AS SUPPORT IN GAS CHROMATOGRAPHY, (column 200 cm × 2 mm, temperature 230 ºC, N_2 flow 40 mL/min, inject temperature 270 ºC, V= 0.4 µL)

Pharmaceutical forms	Guaifenesine quantity (mg/100 mL)	*Concentration of guaifenesine (mg/100 mL)	
		$\overline{C}$	RSD %
Toplexil (syrup) Saidal, subsidiary pharmal, Algeria	666	674	2.9
Toplexil (syrup) Oubari, Syria	666	665	2.9

*Average of 5 determinations.

Determination of phenobarbital: The following conditions were applied for the determination of phenobarbital (**Scheme-II**) using gas chromatography technique.



m.f. = $C_{12}H_{12}N_2O_3$, m.w. = 233.24

Scheme-II: Structure of phenobarbital

Column dimension: 2 mm × 200 cm; Support: Algerian bentonite, mesh: 125-150 µm, specific surface 12 m^2/g and grafted with silicone SE-52; Oven temperature: 240 °C; Gas vector flow: 40 mL/min (N_2 pure); Injection temperature: 270 ºC.

In order to determine phenobarbital in all samples and standards, gas chromatography column was packed with grafted Algerian bentonite (B_{1100}) and SE-52 as a support. The separation of extracted phenobarbital was completely isolated with high sensitivity. The retention time of phenobarbital was 4.71 min. A calibration curve was constructed by the standard procedure. Good linearity (S = 9771.9x + 521.6, R^2 = 0.9990; x = m, mg (phenobarbital)/10 mL and y = S, area of peak) was obtained within the range 10-120 mg (phenobarbital)/10 mL (Fig. 2). All the pharmaceutical separated formulations results of the phenobarbital are summarized in Table-3 and Fig. 3. Finally, it should be mentioned that the injected quantity for both standard solutions and samples was 1.0 µL.

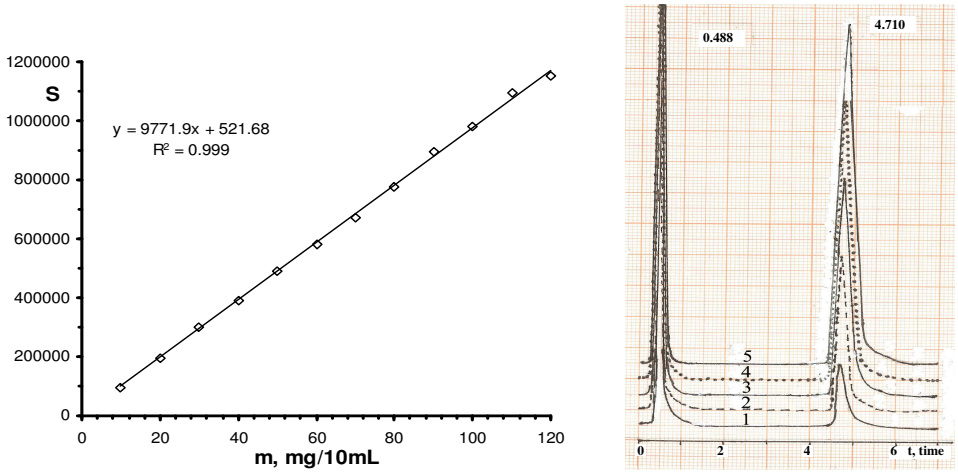


Fig. 2. Determination and separation of phenobarbital using Algerian bentonite (B_{1100}) grafted with SE-52 as support in gas chromatography: (1-5) standard 20, 50, 70, 90 and 110 mg/10 mL, (column 200 cm × 2 mm, temperature 240 ºC, N_2 flow 40 mL/min, inject temperature 270 ºC, V= 1.0 µL)

TABLE-3
DETERMINATION OF PHENOBARBITAL IN PHARMACEUTICALS USING ALGERIAN BENTONITE (B_{1100}) GRAFTED WITH SE-52 AS SUPPORT IN GAS CHROMATOGRAPHY,(column 200 cm × 2 mm, temperature 240 ºC, N_2 flow 40 mL/min, inject temperature 270 ºC, V= 1.0 µL)

Pharmaceutical formulations	Phenobarbital quantity (mg/tablet)	*Concentration of Phenobarbital (mg/tablet)	
		$\overline{C}$	RSD %
Aparoxal (Algeria)	100	100.4	2.6
Dimabarbital (Syria)	100	100.0	2.6
Phenotal-30 (Iran)	30	30.4	2.8
Phenotal-60 (Iran)	60	60.8	2.7

*Average of 5 determinations.

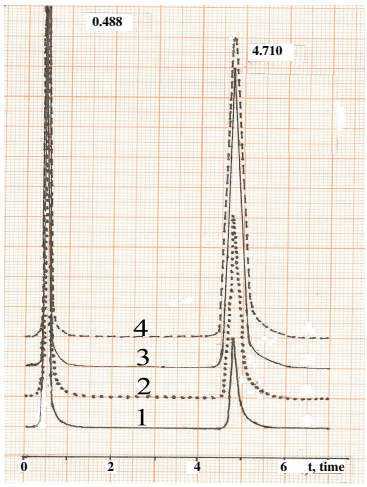


Fig. 3. Determination and separation of phenobarbita using algerian bentonite (B_{1100}) grafted with silicone SE-52 as support in gas chromatography: 1- Phenotal - 30 (Iran, 30 mg/tablet); 2-Phenotal - 60 (Iran, 60 mg/tablet); 3-Aparoxal (Algeria, 100 mg/tablet); 4-Dimabarbital (Syria, 100 mg/tablet), (column 200 cm × 2 mm, temperature 240 ºC, N_2 flow 40 mL/min, inject temperature 270 ºC, V = 1.0 µL)

Conclusion

The separation of two pharmaceutical constituents *i.e.*, guaifenesine and phenobarbital were carried out in both standard and different commercial pharmaceutical formulations using Algerian bentonite (B_{1100}) grafted with silicone SE-52 as support. The determination was achieved using gas chromatography technique. The developed method of analysis gives high precision and reproducibility with relative standard deviation of 2.9 %.

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