

Determination of Some Pharmaceutical Compounds Using Silanized Algerian Bentonite (B₁₁₀₀) as Support in Gas Chromatographic Analysis

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Some pharmaceutical compounds such as butoform, caffeine, menthol, methyl paraben, phenol, propyl paraben and nabumeton were determined using support on the basis of Algerian bentonite in gas chromatographic analysis. The support was prepared by thermal treatment at 1100 °C and chemically by 6 N HCl (B₁₁₀₀). The B₁₁₀₀ granules, with diameter range 125-150 µm and specific surface area 12 m²/g, were silanized with dimethylchlorosilane. The results were characterized by high accuracy and sensitivity with relative standard deviation not exceeding 4.7 %.

Key Words: Determination, Pharmaceutical compounds, Algerian bentonite, Gas chromatographic analysis.

INTRODUCTION

Pharmaceutical compounds were determined by different methods¹. Gas chromatographic analysis was used for determining some pharmaceutical compounds, *e.g.*, menthol¹⁻⁵, methyl paraben and propyl paraben¹⁻⁶, caffeine^{1,7-10} and phenol^{1,11-14}. Whereas, the HPLC method was applied for determining of butoform and nabumeton^{1,15}.

Some chromatographic supports were prepared from siliceous or natural origin materials such as diatomaceous earth or bentonite. Acid wash treatment by HCl removes all soluble oxides from the surface of the support. Modification of the support surface by reaction with silanol groups was carried out by means of chlorosilane compounds as reactants, or by condensation of a suitable polymer as PEG-20M, SE-30 and OV-101¹⁶⁻²².

The natural Algerian bentonite was thermally treated at 1100 °C then refluxed with 6 N HCl (B₁₁₀₀). The B₁₁₀₀ material is composed of the cristobalite, spinal and a small quantity of quartz. The surface area (S_{BET}) of (B₁₁₀₀) is 12 m²/g^{23,24}.

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Chromatographic supports from Algerian bentonite (B₆₅₀ and B₁₁₀₀) were prepared^{25,26}. The two above supports granules, with diameter range 125-150 μm , were modified by silanization with dimethylchlorosilane at 120 °C, under a little flow of nitrogen to avoid the oxidation of dimethylchlorosilane^{25,26}. The support from silanized Algerian bentonite (B₁₁₀₀) was used²⁷ for determination C₅-C₁₈.

EXPERIMENTAL

The chromatograms were obtained by using a GC-9A gas chromatograph equipped with a flame ionization detector (FID) and printer C-R3A (Shimadzu), 1 and 10 μL syringe (Hamilton) and special reactor for grafting. All solvents and chemicals were extra pure grade. The bentonite comes from Roussel quarry, near Maghnia town (northwest Algeria). Stainless steel columns (200 cm \times 2 mm) packed with silanized Algerian bentonite (B1100) were used. Pure nitrogen was used as carrier gas at flow rate 35 mL/min, the inject port temperature: 220-250 °C.

Pharmaceutical compounds: Butoform (butyl 4-aminobenzoate C₁₁H₁₅NO₂, m.w. 193.25 g), caffeine (C₈H₁₀N₄O₂, m.w. 194.19 g), menthol (C₁₀H₂₀O, m.w. 156.27 g), methyl paraben (C₈H₈O₃, m.w. 152.15 g), phenol (C₆H₆O, m.w. 94.11 g), propyl paraben (C₁₀H₁₂O₃, m.w. 180.20 g) and nabumeton (C₁₅H₁₆O₂, m.w. 228.29 g) were used. All these pharmaceutical compounds were extracted by CHCl₃ from standards and pharmaceutical formulations: Hemoride (Sandi Pharma, Syria) each suppository contained: 25 mg butoform; cafalgine (Oubari Pharma, Syria) each tablet contained: 50 mg caffeine, midron extra (Jordan) each tablet contained: 60 mg caffeine, new cetamol 500 (Elsaad Pharma, Syria) each tablet contained: 65 mg caffeine, asia migrine (Asia, Syria) each tablet contained: 100 mg caffeine; palergot-C (Balsam Pharma, Syria) each tablet contained: 100 mg caffeine; sinaseptic (Avecenna Labs., Syria) mouthwash, each 10 mL contained: 4 mg menthol and 50 mg phenol, phenoseptic (Arak, Syria) each 10 mL contained: 4 mg menthol and 25 mg phenol; baby spasm (Sandi Pharma, Syria) drops for children, each 20 mL contained: 2 mg menthol, 16 mg methyl paraben and 4 mg propyl paraben, muco (Sandi Pharma, Syria) each 20 mL contained: 6.7 mg menthol, 6 mg methyl paraben and 4 mg propyl paraben, acidex (Sandi Pharma, Syria) each 20 mL contained: 5 mg menthol, 16 mg methyl paraben and 4 mg propyl paraben, nystatin asia (Asia, Syria) each 20 mL contained: 12 mg methyl paraben and 12 mg propyl paraben and albendazol (Sandi Pharma, Syria) each 20 mL contained: 6 mg methyl paraben and 4 mg propyl paraben, relafen 500 (USA) nonsteroidal antiinflammatory drug (NSAID), each tablet contained: 500 mg nabumeton and nabugesic 500 (Jordan) nonsteroidal antiinflammatory drug (NSAID), each tablet contained: 500 mg nabumeton.

RESULTS AND DISCUSSION

Determination of butoform using the packed column with dimethylchlorosilane (B_{1100}) was suitable for extracted standard and sample, (Fig. 1). In all separations, we obtained completely separated peaks, with high sensitivity and reproducibility. The separation time of butoform was 3.451 min. A calibration curve was constructed by the standard procedure. Good linear relationship ($S = 7581.8 m + 6050$, $R^2 = 0.9969$) was observed within the range 15-30 mg (butoform)/supp. (Fig. 1).

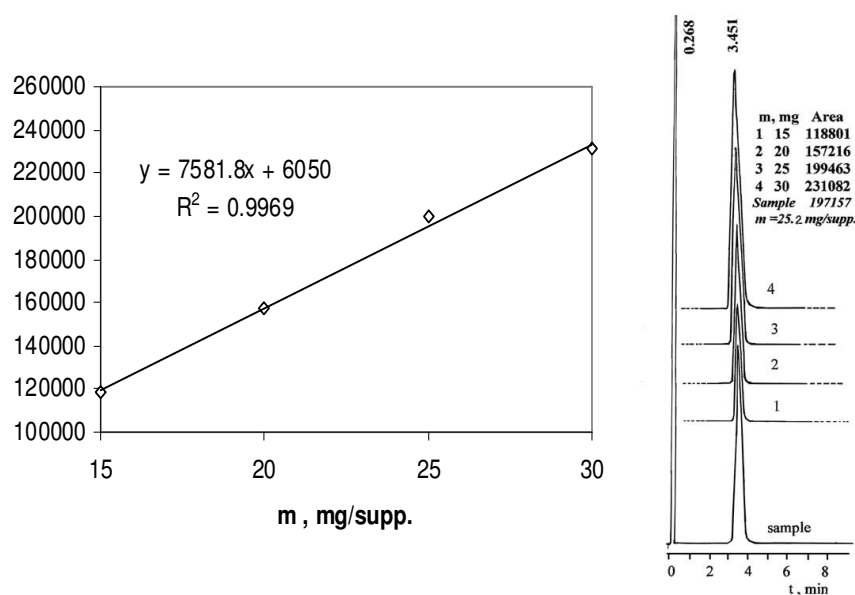


Fig. 1. Determination of butoform using silanized Algerian bentonite (B_{1100}) as support in gas chromatographic analysis, column (200 cm \times 2 mm), temperature 220 $^{\circ}$ C, N_2 flow 35 mL/min, inject port temperature 250 $^{\circ}$ C, $V = 0.5 \mu$ L

Determination of caffeine using the packed column with dimethylchlorosilane (B_{1100}) was suitable for extracted standard and sample. Completely separated peaks, with high sensitivity and reproducibility were obtained. The separation time of caffeine was 3.451 min. A calibration curve was constructed by the standard procedure. Good linear relationship ($S = 5099.6 m + 565.5$, $R^2 = 0.9998$) was observed within the range 25-100 mg (caffeine)/tablet (Fig. 2).

Determination of menthol, methyl paraben and propyl paraben using the packed column with dimethylchlorosilane (B_{1100}) were suitable for extracted standard and sample. Completely separated peaks, with high sensitivity and reproducibility were obtained. The separation times of menthol,

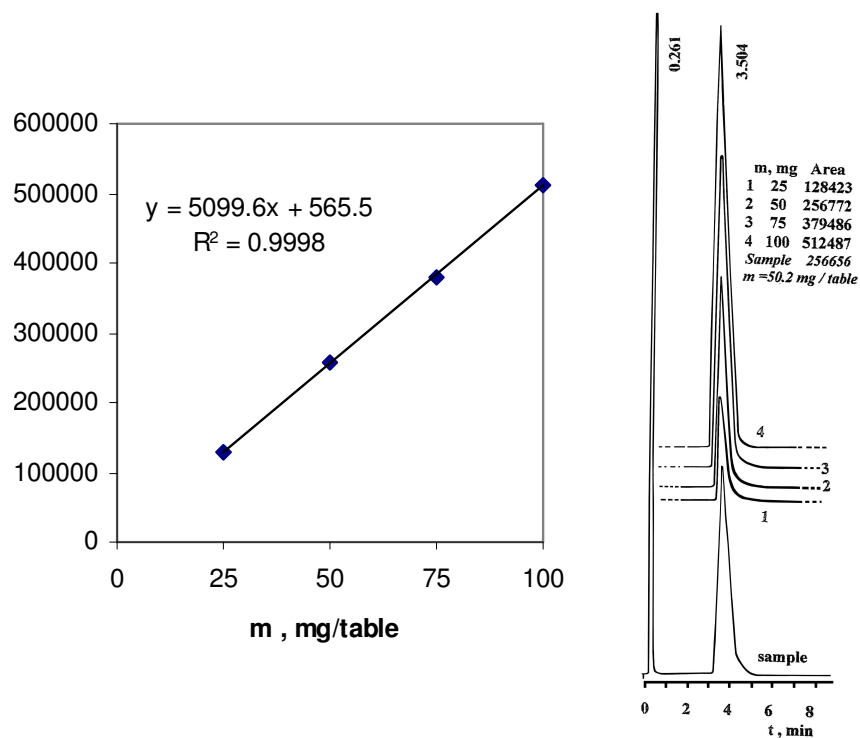


Fig. 2. Determination of caffeine using silanized Algerian bentonite (B_{1100}) as support in gas chromatographic analysis, column (200 cm \times 2 mm), temperature 220 $^{\circ}$ C, N_2 flow 35 mL/min, inject port temperature 250 $^{\circ}$ C, $V = 0.5 \mu\text{L}$

methyl paraben and propyl paraben were 1.140, 3.031 and 5.824 min, respectively. Calibration curves were constructed by the standard procedure. Good linear relationships ($S_1 = 33551 m + 543$, $R^2 = 0.9999$; $S_2 = 21833 m + 1484.5$, $R^2 = 0.9998$ and $S_3 = 24389 m - 5049$, $R^2 = 0.9962$) were observed within the range 1-4 mg (menthol)/10 mL, 5-17 mg (methyl paraben)/10 mL and 4-16 mg (propyl paraben)/10 mL (Fig. 3).

Determination of nabumeton using the packed column with dimethylchlorosilane (B_{1100}) was suitable for extracted standard and sample. Completely separated peaks, with high sensitivity and reproducibility were obtained. The separation time of nabumeton was 3.871 min. Calibration curve was constructed by the standard procedure. Good linear relationship ($S = 1100 m + 9820.7$, $R^2 = 0.9976$) was observed within the range 400-700 mg (nabumeton)/tablet (Fig. 4).

Determination of phenol and menthol using the packed column with dimethylchlorosilane (B_{1100}) were suitable for extracted standard and sample. Completely separated peaks, with high sensitivity and reproducibility were obtained.

Name	a		b		d		c	
	m, mg	Area	m, mg	Area	m, mg	Area	m, mg	Area
Menthol	1	33801	2	67770	3	101824	4	134286
MeParaben	5	110402	10	220954	15	326478	17	374256
PrParaben	4	95335	8	191345	12	276580	16	392113
<i>t</i> , min								
Menthol (1)			MeParaben (2)			PrParaben (3)		
1.140			3.031			5.824		
Sample, Baby Spasm								
2.04 mg			15.97 mg			4.06 mg		

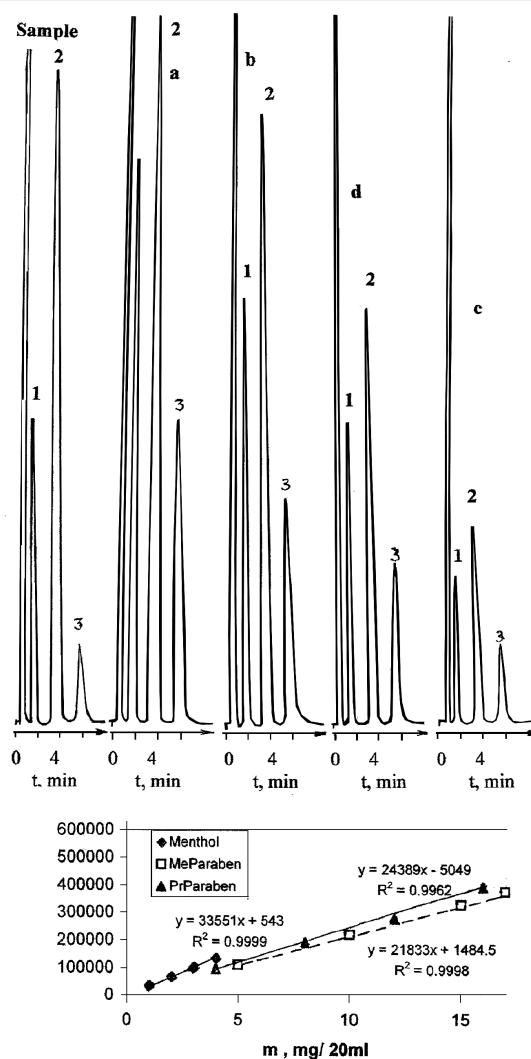


Fig. 3. Determination of menthol, methyl paraben and propyl paraben using silanized Algerian bentonite (B_{100}) as support in gas chromatographic analysis, column ($200\text{ cm} \times 2\text{ mm}$), temperature program ($120\text{--}205\text{ }^{\circ}\text{C}$; $9\text{ }^{\circ}\text{C}/\text{min}$), N_2 flow $35\text{ mL}/\text{min}$, inject port temperature $250\text{ }^{\circ}\text{C}$, $V = 0.5\text{ }\mu\text{L}$.

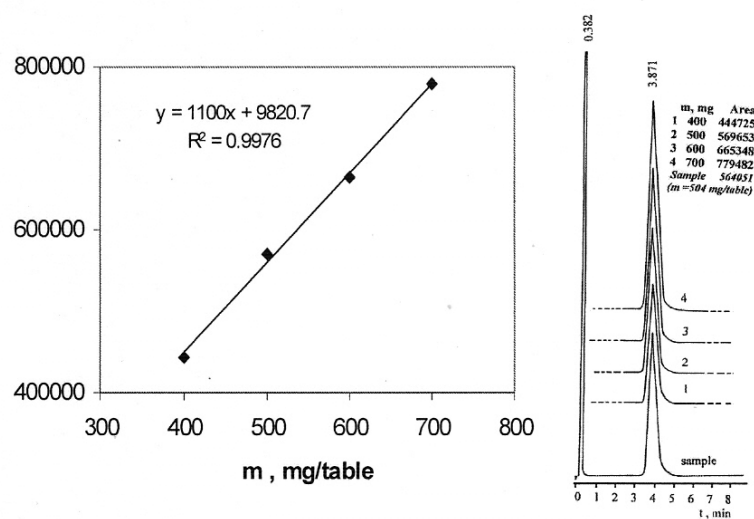


Fig. 4. Determination of nabumeton using silanized Algerian bentonite (B_{1100}) as support in gas chromatographic analysis, column (200 cm \times 2 mm), temperature 220 $^{\circ}$ C, N_2 flow 35 mL/min, inject port temperature 250 $^{\circ}$ C, $V = 0.5 \mu$ L

The separation time of phenol and menthol were 0.626 and 1.253 min, respectively. Calibration curves were constructed by the standard procedure. Good linear relationships ($S = 17339 m + 832.5$, $R^2 = 0.9993$ for phenol and $S = 30063 m + 446.8$, $R^2 = 0.9985$ for menthol) were observed within the range 30-60 mg (phenol)/10 mL and 2-5 mg (menthol)/10 mL (Fig. 5).

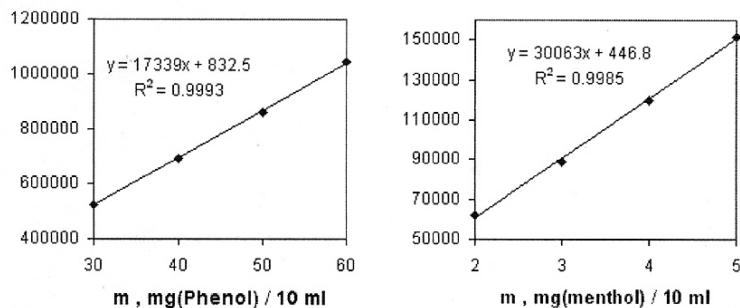


Fig. 5. Calibration curves for determination of phenol and menthol using silanized Algerian bentonite (B_{1100}) as support in gas chromatographic analysis, column (200 cm \times 2 mm), temperature 180 $^{\circ}$ C, N_2 flow 35 mL/min, inject port temperature 220 $^{\circ}$ C, $V = 0.5 \mu$ L

Determination of pharmaceutical compounds: Butoform, caffeine, menthol, phenol, methyl paraben, propyl paraben and nabumeton using silanized Algerian bentonite (B₁₁₀₀) as support in gas chromatographic analysis gave high accurate and sensitive results, with relative standard deviation not exceeding 4.7 % (Tables 1-5).

TABLE-1
DETERMINATION OF BUTOFORM (IN SUPPOSITORIES,
HEMORIDE) USING SILANIZED ALGERIAN BENTONITE (B₁₁₀₀)
AS SUPPORT IN GAS CHROMATOGRAPHIC ANALYSIS, COLUMN
(200 cm × 2 mm), TEMPERATURE 220 °C, N₂ FLOW 35 mL/min,
INJECT PORT TEMPERATURE 250 °C, V = 0.5 µL

Taken (mg)	Found (mg)	RSD (%)
15.00	14.87	4.1
20.00	19.94	3.8
25.00	25.51	3.5
30.00	29.68	3.2
Sample, hemoride (25 mg/supp.)	25.20	3.5

TABLE-2
DETERMINATION OF CAFFEINE (IN SOME PHARMACEUTICAL
FORMULATIONS) USING SILANIZED ALGERIAN BENTONITE
(B₁₁₀₀) AS SUPPORT IN GAS CHROMATOGRAPHIC ANALYSIS,
COLUMN (200 cm × 2 mm), TEMPERATURE 220 °C, N₂ FLOW 35
mL/min, INJECT PORT TEMPERATURE 250 °C, V = 0.5 µL

Taken (mg)	Found (mg/tablet)	RSD (%)
25.00	25.07	3.4
50.00	50.24	3.3
75.00	74.30	3.1
100.00	100.38	2.9
Sample 1, cafalgine (50mg/tablet)	50.20	3.3
Sample 2, midron extra (60mg/ tablet)	60.20	3.2
Sample 3, new cetamol 500 (65 mg/tablet)	65.10	3.2
Sample 4, asia migraine (100 mg/tablet)	100.20	3.0
Sample 5, palergot-C (100mg/tablet)	99.80	3.0

TABLE-3
 DETERMINATION OF MENTHOL, METHYL PARABEN AND PROPYL
 PARABEN (IN SOME PHARMACEUTICAL FORMULATIONS) USING
 SILANIZED ALGERIAN BENTONITE (B₁₁₀₀) AS SUPPORT IN GAS
 CHROMATOGRAPHIC ANALYSIS, COLUMN (200 cm × 2 mm),
 TEMPERATURE PROGRAM (120-205 °C; 9 °C/min), N₂ FLOW
 35 mL/min, INJECT PORT TEMPERATURE 250 °C, V = 0.5 µL

Determined compound	Taken (mg)	Found (mg)	RSD (%)
Menthol	1.00	0.99	4.2
	2.00	2.00	4.1
	3.00	3.02	3.9
	4.00	3.99	3.8
	Sample 1, Baby spasm (2 mg/20 mL) (V = 20 mL)	1.99	4.1
	Sample 2, Muco (6.7mg/20 mL) (V = 10 mL)	6.57	3.9
	Sample 3, Acidex (5mg/20 mL) (V = 10 mL)	4.98	4.0
Methyl paraben	5.00	4.99	3.0
	10.00	10.05	2.8
	15.00	14.89	2.6
	17.00	17.07	2.5
	Sample 1, Baby spasm (16 mg/20 mL) (V = 20 mL)	15.97	2.6
	Sample 2, Muco (6 mg/20 mL) (V = 20 mL)	6.02	3.0
	Sample1, Acidex (16 mg/20 mL) (V = 20 mL)	16.06	2.7
	Sample 1, Nystatin asia (12 mg/20 mL) (V = 20 mL)	12.03	2.8
Sample 1, Albendazol (6 mg/20 mL) (V = 20 mL)	5.98	3.0	
Propyl paraben	4.00	4.11	4.7
	8.00	8.05	4.5
	12.00	11.55	4.4
	16.00	16.28	4.3
	Sample1, Baby spasm (4 mg/20 mL) (V = 20 mL)	4.06	4.7
	Sample 2, Muco (4 mg/20 mL) (V = 20 mL)	3.99	4.7
	Sample 3, Acidex (4 mg/20 mL) (V = 20 mL)	4.03	4.7
	Sample 4, Nystatin asia (12 mg/20 mL) (V = 20 mL)	11.96	4.7
Sample 5, Albendazol (4 mg/20 mL) (V = 20 mL)	4.01	4.7	

TABLE-4
 DETERMINATION OF NABUMETON (IN SOME PHARMACEUTICAL
 FORMULATIONS) USING SILANIZED ALGERIAN BENTONITE (B₁₁₀₀)
 AS SUPPORT IN GAS CHROMATOGRAPHIC ANALYSIS, COLUMN
 (200 cm × 2 mm), TEMPERATURE 220 °C, N₂ FLOW 35 mL/min,
 INJECT PORT TEMPERATURE 250 °C, V = 0.5 µL

Taken (mg)	Found (mg)	RSD (%)
400	395	4.8
500	509	4.7
600	596	4.7
700	700	4.6
Sample, Relafen 500 (500 mg/tablet)	504	4.7
Sample, Nabugesic 500 (500 mg/tablet)	502	4.7

TABLE-5
 DETERMINATION OF PHENOL AND MENTHOL
 (IN SOME PHARMACEUTICAL FORMULATIONS) USING
 SILANIZED ALGERIAN BENTONITE (B₁₁₀₀) AS SUPPORT IN
 GAS CHROMATOGRAPHIC ANALYSIS, COLUMN (200 cm × 2 mm),
 TEMPERATURE 180 °C, N₂ FLOW 35 mL/min, INJECT PORT
 TEMPERATURE 220 °C, V = 0.5 µL

Determined compound	Taken (mg)	Found (mg)	RSD (%)
Phenol	30.0	30.3	3.4
	40.0	39.9	3.3
	50.0	50.0	3.1
	60.0	59.8	3.0
	Sample 1, Sinaseptic (50 mg/10 mL) (V = 10 mL)	50.1	3.1
	Sample 2, Phenoseptic (25 mg/10 mL) (V = 20 mL)	25.3	3.4
Menthol	2.00	2.02	4.2
	300	2.97	4.1
	4.00	3.95	3.9
	5.00	5.06	3.8
	Sample 1, Sinaseptic (4 mg/10 mL) (V = 10 mL)	3.98	3.9
	Sample 2, Phenoseptic (4 mg/10 mL) (V = 10 mL)	3.99	3.9

Conclusion

The prepared support dimethylchlorosilane silanized B₁₁₀₀ showed good separated peaks in determining the different pharmaceutical compounds such as butoform, caffeine, menthol, phenol, methyl paraben, propyl paraben and nabumeton with good reproducibility and sensitivity.

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