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Research Article

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Synthesis and spectrochemical study of some Albendazole derivatives

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ABSTRACT

*The Albendazole is the drug of reference in the medical treatment of hydatidosis, but its efficacy is limited by its poor bioavailability. Two series of ester and amide potential prodrugs of albendazole (**1a-d** and **2a-f**) were synthesized. Other set of the new benzimidazole derivatives as alkyl derivatives were synthesized from the albendazole **3a-j**. The compounds thus prepared were characterized by their physical (TLC) and spectral data (IR and NMR).*

Keywords: Benzimidazole, Albendazole, Prodrug, Synthesis.

INTRODUCTION

The hydatidosis is a cosmopolitan parasitic disease that stays a real public health problem in the countries of strong endemic. The treatment essentially calls on the surgery that includes morbidity and mortality significant, from where the interest to develop the medical treatment whose main representative is the albendazole. The efficiency of this molecule is proven but limited by its bad biodisponibility due to its weak absorption by the organism [1-2].

The development of medical treatment is important because chemotherapy can be used in patients of all ages and it is less constrained by the condition of patients than surgery [3]. To find effective chemotherapy that can improve the care of patients with this infection, several drugs have been tried, even those who had limited effect and it is only with the benzimidazole carbamates that the practice of chemotherapy was possible.

Albendazole (ALB) is a typical, broad spectrum benzimidazole antiparasitic agent [4], first approved for human use in 1982. ALB is relatively insoluble in water and most organic solvents, properties that influence its absorption and behaviour in the body. As it undergoes very rapid first pass metabolism in all species, the unchanged drug has not been reliably detected in plasma. Plasma levels of the initial oxidised metabolites (the sulphoxide and sulphone) in all species are much higher than of the parent drug. The sulphoxide is generally considered to be the active metabolite responsible for the therapeutic activity of ALB [5-7].

Several studies have aimed to increase the absorption of albendazole to obtain optimal serum concentrations of albendazole sulfoxide, as active metabolite, by galenic devices (emulsion or liposome), or by taking this molecule during a meal rich in lipids [8-9]. Other authors have reported the prodrugs of albendazole as amides or esters derivatives to improve the absorption of this molecule. In this paper we reported three series of the new albendazole derivatives with promising antiparasitic activity.

EXPERIMENTAL SECTION

Synthesis

All reactions were followed by TLC 0.25 mm silica gel plates (Ethyl acetate / Hexane: 7/3).

General procedure for the synthesis of ester derivatives 1a-d (Fig.1)

Keep stirring the mixture for 2 hours of albendazole and potassium bicarbonate ($KHCO_3$) in acetone. Add slowly the appropriate chloride formiate and let stir for 24 hours. Remove the solvent and the residue taken up in a minimum of water and extracted with dichloromethane. Recrystallized from hexane.

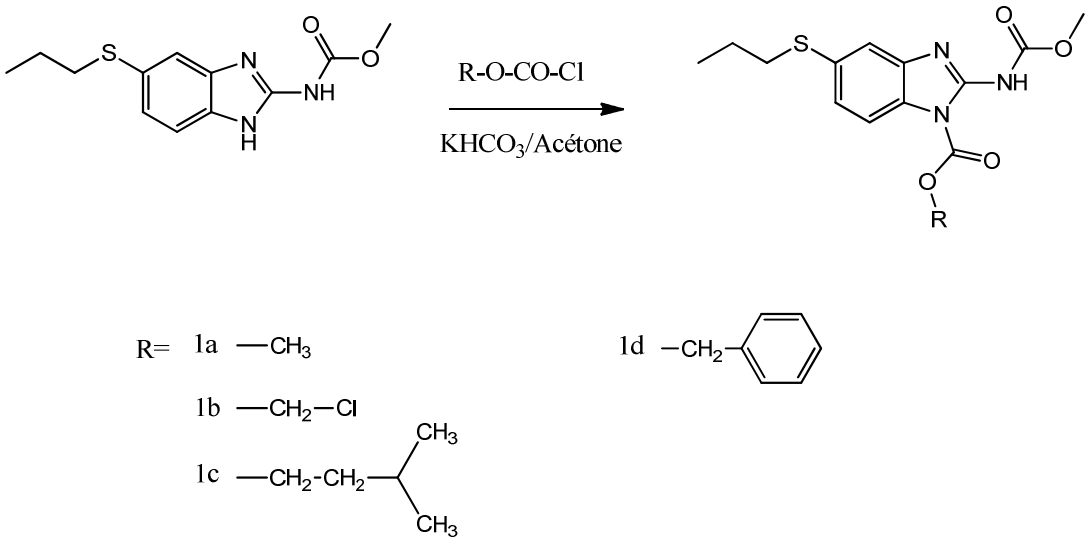


Figure 1 : Scheme of the ester derivatives of albendazole

General procedure for the synthesis of amide derivatives 2a-f (Fig.2)

Suspension of albendazole (ABZ) in tetahydrofuran (THF) was mixed with an equivalent of sodium hydride and stirred for 3 hours. The aromatic acyl chloride was added and stirred for 24 hours. The THF is removed under vaccuo, the residue is washed, extracted with dichloromethan and recrystallised from dichloromethan - hexane.

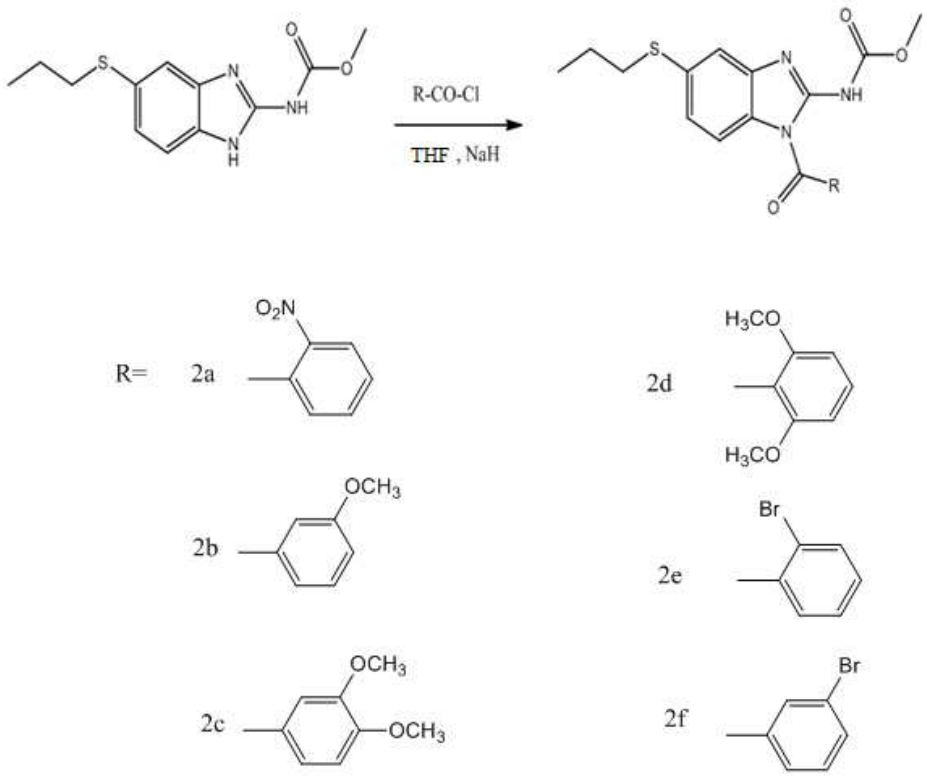
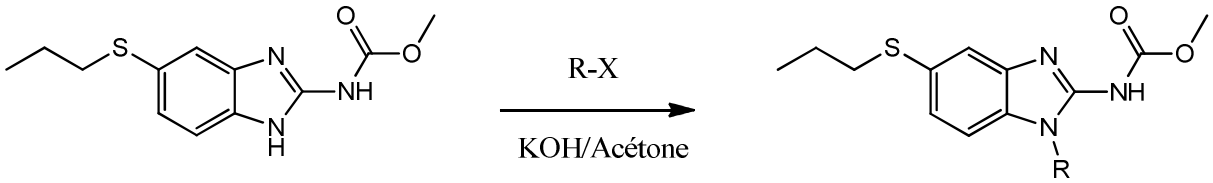


Figure 2 : Scheme of the amide derivatives of albendazole

General procedure for the synthesis of alkyl derivatives 3a-j (Fig.3)

Keep under stirring for two hours the mixture of albendazole and potassium hydroxide (KOH) in acetone. Add slowly the appropriate alkyl halide (RX) and let stir for 24 hours. Remove the solvent and the residue taken up in a minimum of water and extracted with dichloromethane. Recrystallized from hexane.



R= 3a —CH_3

3b —CH_2-CH_3

3c —CH_2-CH_2—CH_3

3d —CH_2-CH_2-CH_2—CH_3

3e —CH_2-CH_2-CH_2-CH_2-CH_3

3f —CH_2-CH_2-CH_2-CH_2-CH_2-CH_2-OH

3g —CH_2-CH(CH_3)-CH_3

3h —CH_2-C(=O)-O-CH_2-CH_3

3i —CH_2-CH(O)-CH_2

3j —CH_2-CH(OH)-CH_2-OH

Figure 3 : Scheme of the alkyl derivatives of albendazole

Spectrochemical study

FTIR spectroscopy

The IR spectrum of the derivatives was measured, using an FTIR spectrophotometer (Jasco FT/IR-460 plus) using KBr pelleting. The scans were executed from 4000 cm^{-1} to 500 cm^{-1}.

^{1}H NMR spectroscopy

The ^{1}H NMR spectrum of the derivatives was recorded at 25° using the NMR spectrometer (AVANCE 300 Bruker) employing DMSO-d_6 as a solvent. The H^1 NMR chemical shifts ($\Delta\delta$) are expressed in ppm relative to tetramethylsilane (TMS) used as reference (TMS $\delta = 0$). Coupling constants J are expressed in Hz.

RESULTS AND DISCUSSION

The poor bioavailability of albendazole is due to its lipophilicity, in fact it is practically insoluble in water and insoluble in most organic solvents. Thus it has been classified according to the Biopharmaceutics Classification System (BCS) in class IV (poorly soluble, poorly permeable) where the interest of the research of novels anti-hydatid cysts [10].

The design of prodrugs by chemical approach is usually done by the synthesis of derivatives easily metabolizable as esters or amides. The main interest is to modify the physicochemical properties of the molecule being studied to increase its bioavailability. Some albendazole prodrugs have been reported in the literature as ester and amide derivatives [11-14]. In this aproach the series **1a-d** and **2a-f** that we synthesized were designed as potential prodrugs. On the other hand it was shown that the hydrogen of the nitrogen n°1 of albendazole is important for scolicidal activity, but it is not essential [15]. Thus the set **3a-j** has been designed to contribute to the arsenal of derivatives with potential antiparasitic activity.

Perspective in these products will be a study of the bioavailability and the scolicidal activity against the cysts of *Echinoccocus granulosus*.

The structures of synthesized derivatives were confirmed by infra red IR and ^{1}H NMR:

Methyl (1-(methoxycarbonyl)-5-(propylthio)-benzimidazol-2-yl) carbamate 1a
IR (KBr) : v 2959, 2337, 1751, 1623, 1589, 1441,1272, 1225, 1091 cm^{-1}. ^{1}H NMR (300 MHz, DMSO-d6) δ 0,92 (t, 3H, C**H$_3$**-CH$_2$-CH$_2$-S) ; δ 1,52 (m, 2H, CH$_3$-C**H$_2$**-CH$_2$-S) ; δ 2,83 (t, 2H, CH$_3$-CH$_2$-C**H$_2$**-S) ; δ 3,74 (s, 3H, -OC**H$_3$**) ; δ 3,94 (s, 3H, -OC**H$_3$**) ; δ 7,09 (dd, J = 9 Hz,1H, H-5) ; δ 7,33 (d, J = 9 Hz, 1H, H-4) ; δ 7,39 (d, J = 2 Hz, 1H, H-7); δ 11,69 (s, 1H, -N**H**CO-).

Chloromethyl 2-((methoxycarbonyl)amino)-5-(propylthio)- benzimidazol-2-yl) carbamate 1b
IR (KBr) : v 2958, 1754, 1665, 1580, 1438,1240, 1194, 1044 cm^{-1}; ^{1}H NMR (300 MHz, DMSO-d6) δ 0,92 (t, 3H, C**H$_3$**-CH$_2$-CH$_2$-S) ; δ 1,52 (m, 2H, CH$_3$-C**H$_2$**-CH$_2$-S) ; δ 2,83 (t, 2H, CH$_3$-CH$_2$-C**H$_2$**-S) ; δ 3,74 (s, 3H, -OC**H$_3$**) ; δ 6,20 (s, 2H, -O-C**H$_2$**-Cl) ; δ 7,09 (dd, J = 9 Hz,1H, H-5) ; δ 7,33 (d, J = 9 Hz, 1H, H-4) ; δ 7,39 (d, J = 2 Hz, 1H, H-7); δ 11,69 (s, 1H, -N**H**CO-)

Isobutyl 2-((methoxycarbonyl)amino)-5-(propylthio)- benzimidazol-2-yl) carbamate 1c
IR (KBr) : v 2961, 1868, 1741, 1650, 1458,1334, 1243, 1106, 1019 cm^{-1}. ^{1}H NMR (300 MHz, DMSO-d6) δ 0,85 (d, J = 2 Hz, 3H, (C**H$_3$**)$_2$-CH-CH$_2$) ; δ 0,92 (t, 3H, C**H$_3$**-CH$_2$-CH$_2$-S) ; δ 1,52 (m, 2H, CH$_3$-C**H$_2$**-CH$_2$-S) ; δ 1,82 (m, 1H, (CH$_3$)$_2$-C**H**-CH$_2$); δ 2,83 (t, 2H, CH$_3$-CH$_2$-C**H$_2$**-S) ; δ 3,74 (s, 3H, -OC**H$_3$**) ; δ 3,92 (d, J = 2 Hz, 2H, (CH$_3$)$_2$-CH-C**H$_2$**) ; δ 7,09 (dd, J = 9 Hz,1H, H-5) ; δ 7,33 (d, J = 9 Hz, 1H, H-4) ; δ 7,39 (d, J = 2 Hz, 1H, H-7); δ 11,69 (s, 1H, -N**H**CO-)

Benzyl 2-((methoxycarbonyl)amino)-5-(propylthio)- benzimidazol-2-yl) carbamate 1d
IR (KBr) : v 2958, 2336, 1730, 1622, 1588, 1445, 1226, 1195, 1096 cm^{-1}. ^{1}H NMR (300 MHz, DMSO-d6) δ 0,92 (t, 3H, C**H$_3$**-CH$_2$-CH$_2$-S) ; δ 1,52 (m, 2H, CH$_3$-C**H$_2$**-CH$_2$-S) ; δ 2,83 (t, 2H, CH$_3$-CH$_2$-C**H$_2$**-S) ; δ 3,74 (s, 3H, -OC**H$_3$**) ; δ 5,44 (s, 2H, -O-C**H$_2$**-Ar) ; δ 7,09 (dd, J = 9 Hz,1H, H-5) ; δ 7,33 (d, J = 9 Hz, 1H, H-4) ; δ 7,39 (d, J = 2 Hz, 1H, H-7); δ 7,41 (dd, J = 9 Hz, 1H, H-4'); δ 7,48 (dd, J = 9 Hz, 1H, 1H, H-3'); δ 7,64 (d, J = 2 Hz, 1H, H-2'); δ 11,69 (s, 1H, -N**H**CO-).

Methyl (1-(2-nitrobenzoyl)-5-(propylthio)-benzimidazol-2-yl) carbamate 2a
IR (KBr) : v 2956, 2854, 1606,1572, 1526, 1392, 1270, 1075 cm^{-1}.^{1}H NMR (300 MHz, DMSO-d6) δ 0,92 (t, 3H, C**H$_3$**-CH$_2$-CH$_2$-S) ; δ 1,52 (m, 2H, CH$_3$-C**H$_2$**-CH$_2$-S) ; δ 2,89 (t, 2H, CH$_3$-CH$_2$-C**H$_2$**-S) ; δ 3,83 (s, 3H, -OC**H$_3$**) ; δ 7,27 (dd, J = 9 Hz,1H, H-5) ; δ 7,50 (d, J = 9 Hz, 1H, H-4) ; δ 7,94 (d, J = 2 Hz, 1H, H-7); δ 7,42 (d, J = 9 Hz, 1H, H-3'); δ 8,08 (dd, J = 2 Hz, 1H, H-3'); δ 8,25 (d, J = 2Hz, 1H, H-2'); δ 8,44 (d, J = 2 Hz, 1H, H-4'); δ 11,64 (s, 1H, -N**H**CO-).

Methyl (1-(3-methoxybenzoyl)-5-(propylthio)-benzoimidazol-2-yl) carbamate 2b
IR (KBr) : v 2956, 2924, 1711, 1623,1587, 1443, 1325, 1269, 1095 cm^{-1}. ^{1}H NMR (300 MHz, DMSO-d6) δ 0,92 (t, 3H, C**H$_3$**-CH$_2$-CH$_2$-S) ; δ 1,52 (m, 2H, CH$_3$-C**H$_2$**-CH$_2$-S) ; δ 2,83 (t, 2H, CH$_3$-CH$_2$-C**H$_2$**-S) ; δ 3,74 (s, 3H, -OC**H$_3$**) ; δ 7,09 (dd, J = 9 Hz,1H, H-5) ; δ 7,33 (d, J = 9 Hz, 1H, H-4) ; δ 7,39 (d, J = 2 Hz, 1H, H-7); δ 7,31 (d, J = 2 Hz, 1H, H-4'); δ 7,41 (d, J = 2 Hz, 1H, H-2'); δ 7,66 (dd, J = 2 Hz, 1H, H-3'); δ 11,64 (s, 1H, -N**H**CO-).

Methyl (1-(3,4-dimethoxybenzoyl)-5-(propylthio)-benzimidazol-2-yl)carbamate 2c
IR (KBr) : v 2957, 1789, 1622, 1443,1268, 1095 cm^{-1}. ^{1}H NMR (300 MHz, DMSO-d6) δ 0,92 (t, 3H, C**H$_3$**-CH$_2$-CH$_2$-S) ; δ 1,52 (m, 2H, CH$_3$-C**H$_2$**-CH$_2$-S) ; δ 2,83 (t, 2H, CH$_3$-CH$_2$-C**H$_2$**-S) ; δ 3,74 (s, 3H, -OC**H$_3$**) ; δ 7,09 (dd, J = 9 Hz,1H, H-5) ; δ 7,33 (d, J = 9 Hz, 1H, H-4) ; δ 7,39 (d, J = 2 Hz, 1H, H-7); δ 7,85 (d, J = 9 Hz, 1H, H-2'); δ 8,03 (d, J = 9 Hz, 1H, H-3'); δ 11,64 (s, 1H, -N**H**CO-).

Methyl (1-(2,6-dimethoxybenzoyl)-5-(propylthio)-benzimidazol-2-yl) carbamate 2d
IR (KBr) : v 2956, 2925, 1703, 1636,1593, 1475, 1326, 1255, 1194 cm^{-1}. ^{1}H NMR (300 MHz, DMSO-d6) δ 0,92 (t, 3H, C**H$_3$**-CH$_2$-CH$_2$-S) ; δ 1,52 (m, 2H, CH$_3$-C**H$_2$**-CH$_2$-S) ; δ 2,83 (t, 2H, CH$_3$-CH$_2$-C**H$_2$**-S) ; δ 3,74 (s, 3H, -OC**H$_3$**) ; δ 7,09 (dd, J = 9 Hz,1H, H-5) ; δ 7,33 (d, J = 9 Hz, 1H, H-4) ; δ 7,39 (d, J = 2 Hz, 1H, H-7); δ 6,76 (d, J = 2 Hz, 1H, H-3'); δ 7,50 (d, J = 2 Hz, 1H, H-4'); δ 11,64 (s, 1H, -N**H**CO-).

Methyl (1-(2-bromobenzoyl)-5-(propylthio)-benzimidazol-2-yl) carbamate 2e
IR (KBr) : v 2956, 1731, 1665,1442, 1373, 1204, 1017 cm^{-1}. ^{1}H NMR (300 MHz, DMSO-d6) δ 0,92 (t, 3H, C**H$_3$**-CH$_2$-CH$_2$-S) ; δ 1,52 (m, 2H, CH$_3$-C**H$_2$**-CH$_2$-S) ; δ 2,83 (t, 2H, CH$_3$-CH$_2$-C**H$_2$**-S) ; δ 3,73 (s, 3H, -OC**H$_3$**) ; δ 7,09 (dd, J = 6 Hz,1H, H-5) ; δ 7,33 (d, J = 9 Hz, 1H, H-4) ; δ 7,41 (d, J = 2 Hz, 1H, H-7); δ 7,58 (dd, J = 3 Hz, 1H, H-3'); δ 7,77 (dd, J = 2 Hz, 1H, H-4'); δ 7,95 (d, J = 2 Hz, 1H, H-2'); δ 11,69 (s, 1H, -N**H**CO-).

Methyl (1-(3-bromobenzoyl)-5-(propylthio)-benzimidazol-2-yl) carbamate 2f
Données IR (KBr) : v 2956, 2924, 1631, 1665,1588, 1443, 1269, 1097 cm^{-1}. ^1H NMR (300 MHz, DMSO-d6) δ 0,92 (t, 3H, C**H**$_3$-CH_2-CH_2-S) ; δ 1,52 (m, 2H, CH_3-C**H**$_2$-CH_2-S) ; δ 2,83 (t, 2H, CH_3-CH_2-C**H**$_2$-S) ; δ 3,73 (s, 3H, -OC**H**$_3$) ; δ 7,09 (dd, J = 6 Hz,1H, H-5) ; δ 7,33 (d, J = 9 Hz, 1H, H-4) ; δ 7,41 (d, J = 2 Hz, 1H, H-7); δ 7,18 (dd, J = 3 Hz, 1H, H-3'); δ 7,23 (d, J = 2 Hz, 1H, H-2'); δ 8,48 (s,1H, H-6'); δ 11,69 (s, 1H, -N**H**CO-).

Methyl (1-methyl-5-(propylthio)-benzimidazol-2-yl) carbamate 3a
IR (KBr) : v 2957, 1706, 1622,1447, 1342, 1261, 1161 cm^{-1}. ^1H NMR (300 MHz, DMSO-d6) δ 0,92 (t, 3H, C**H**$_3$-CH_2-CH_2-S) ; δ 1,52 (m, 2H, CH_3-C**H**$_2$-CH_2-S) ; δ 2,83 (t, 2H, CH_3-CH_2-C**H**$_2$-S) ; δ 3,49 (s, 3H, C**H**$_3$-N) ; δ 3,73 (s, 3H, -OC**H**$_3$) ; δ 7,09 (dd, J = 6 Hz,1H, H-5) ; δ 7,33 (d, J = 9 Hz, 1H, H-4) ; δ 7,41 (d, J = 2 Hz, 1H, H-7); δ 11,69 (s, 1H, -N**H**CO-).

Methyl (1-ethyl-5-(propylthio)-benzimidazol-2-yl) carbamate 3b
IR (KBr) : v 2959, 1717, 1613,1518, 1440, 1266, 1083 cm^{-1}. ^1H NMR (300 MHz, DMSO-d6) δ 0,92 (t, 3H, C**H**$_3$-CH_2-CH_2-S) ; δ 1,26 (t, 3H, C**H**$_3$-CH_2-N); δ 1,52 (m, 2H, CH_3-C**H**$_2$-CH_2-S) ; δ 2,83 (t, 2H, CH_3-CH_2-C**H**$_2$-S) ; δ 3,73 (s, 3H, -OC**H**$_3$) ; δ 4,02 (m, 2H, CH_3-C**H**$_2$-N); δ 7,09 (dd, J = 6 Hz,1H, H-5) ; δ 7,33 (d, J = 9 Hz, 1H, H-4) ; δ 7,41 (d, J = 2 Hz, 1H, H-7); δ 11,69 (s, 1H, -N**H**CO-).

Methyl (1-propyl-5-(propylthio)-benzimidazol-2-yl) carbamate 3c
IR (KBr) : v 2957, 1704, 1621,1445, 1322, 1270, 1096 cm^{-1}. ^1H NMR (300 MHz, DMSO-d6) δ 0,92 (t, 3H, C**H**$_3$-CH_2-CH_2-S) ; δ 1,34 (m, 2H, CH_3-C**H**$_2$-CH_2-N) ; δ 1,52 (m, 2H, CH_3-C**H**$_2$-CH_2-S) ; δ 2,83 (t, 2H, CH_3-CH_2-C**H**$_2$-S) ; δ 4,05 (t, 2H, CH_3-CH_2-C**H**$_2$-N) ; δ 3,73 (s, 3H, -OC**H**$_3$) ; δ 7,09 (dd, J = 6 Hz,1H, H-5) ; δ 7,33 (d, J = 9 Hz, 1H, H-4) ; δ 7,41 (d, J = 2 Hz, 1H, H-7); δ 11,69 (s, 1H, -N**H**CO-).

Methyl (1-butyl-5-(propylthio)-benzimidazol-2-yl) carbamate 3d
IR (KBr) : v 2957, 1713, 1632, 1588, 1444, 1224, 1095 cm^{-1}. ^1H NMR (300 MHz, DMSO-d6) δ 0,92 (t, 3H, C**H**$_3$-CH_2-CH_2-S) ; δ 1,25 (m, 2H, CH_3-CH_2-C**H**$_2$-CH_2-N) ; δ 1,52 (m, 2H, CH_3-C**H**$_2$-CH_2-S) ; δ 2,83 (t, 2H, CH_3-CH_2-C**H**$_2$-S) ; δ 3,97 (t, 2H, CH_3-CH_2-CH_2-C**H**$_2$-N) ; δ 3,73 (s, 3H, -OC**H**$_3$) ; δ 7,09 (dd, J = 6 Hz,1H, H-5) ; δ 7,33 (d, J = 9 Hz, 1H, H-4) ; δ 7,41 (d, J = 2 Hz, 1H, H-7); δ 11,69 (s, 1H, -N**H**CO-).

Methyl (1-pentyl-5-(propylthio)-benzimidazol-2-yl) carbamate 3e
IR (KBr) : v 2957, 1631,1589, 1326, 1223, 1096 cm^{-1}. ^1H NMR (300 MHz, DMSO-d6) δ 0,92 (t, 3H, C**H**$_3$-CH_2-CH_2-S) ; δ 1,23 (m, 2H, CH_3-CH_2-C**H**$_2$-CH_2- CH_2-N) ; δ 1,52 (m, 2H, CH_3-C**H**$_2$-CH_2-S) ; δ 1,67 (m, 2H, CH_3-CH_2-CH_2-C**H**$_2$- CH_2-N) ; δ 2,83 (t, 2H, CH_3-CH_2-C**H**$_2$-S) ; δ 3,66 (t, 2H, CH_3-CH_2-CH_2-CH_2-C**H**$_2$-N) ; δ 3,73 (s, 3H, -OC**H**$_3$) ; δ 7,09 (dd, J = 6 Hz,1H, H-5) ; δ 7,33 (d, J = 9 Hz, 1H, H-4) ; δ 7,41 (d, J = 2 Hz, 1H, H-7); δ 11,69 (s, 1H, -N**H**CO-).

Methyl (1-(6-hydroxyhexyl)-5-(propylthio)-benzimidazol-2-yl) carbamate 3f
IR (KBr) : v 2956, 1711, 1631, 1589, 1443, 1326, 1224, 1096 cm^{-1}. ^1H NMR (300 MHz, DMSO-d6) δ 0,92 (t, 3H, C**H**$_3$-CH_2-CH_2-S) ; δ 1,19 (m, 2H, OH-CH_2-CH_2-C**H**$_2$- C**H**$_2$-CH_2- CH_2-N) ; δ 1,52 (m, 2H, CH_3-C**H**$_2$-CH_2-S) ; δ 2,83 (t, 2H, CH_3-CH_2-C**H**$_2$-S) ; δ 3,16 (s, 1H, O**H**-CH_3-CH_2-CH_2-CH_2-CH_2-CH_2-N) ; δ 3,73 (s, 3H, -OC**H**$_3$) ; δ 7,09 (dd, J = 6 Hz,1H, H-5) ; δ 7,33 (d, J = 9 Hz, 1H, H-4) ; δ 7,41 (d, J = 2 Hz, 1H, H-7); δ 11,69 (s, 1H, -N**H**CO-).

Methyl (1-isobutyl-5-(propylthio)-benzimidazol-2-yl) carbamate 3g
IR (KBr) : v 2957, 1631, 1584,1444, 1325, 1270, 1096 cm^{-1}. ^1H NMR (300 MHz, DMSO-d6) δ 0,92 (t, 3H, C**H**$_3$-CH_2-CH_2-S) ; δ 1,52 (m, 2H, CH_3-C**H**$_2$-CH_2-S) ; δ 2,07 (m, 1H, $(CH_3)_2$-C**H**-CH_2-N) ; δ 2,83 (t, 2H, CH_3-CH_2-C**H**$_2$-S) ; δ 3,73 (s, 3H, -OC**H**$_3$) ; δ 3,92 (m, 2H, $(CH_3)_2$-CH-C**H**$_2$-N) ; δ 7,09 (dd, J = 6 Hz,1H, H-5) ; δ 7,33 (d, J = 9 Hz, 1H, H-4) ; δ 7,41 (d, J = 2 Hz, 1H, H-7); δ 11,69 (s, 1H, -N**H**CO-).

Ethyl 2-(2-((methoxycarbonyl)amino)-5-(propylthio)-benzimidazol-1-yl)acetate 3h
IR (KBr) : v 2956, 1629, 1491, 1449, 1365, 1271, 1098 cm^{-1}. ^1H NMR (300 MHz, DMSO-d6) δ 0,92 (t, 3H, C**H**$_3$-CH_2-CH_2-S) ; δ 1,52 (m, 2H, CH_3-C**H**$_2$-CH_2-S) ; δ 1,88 (t, 3H, C**H**$_3$-CH_2-O-CO-CH_2-N) ; δ 2,06 (m, 3H, CH_3-C**H**$_2$-O-CO-CH_2-N) ; δ 2,09 (m, 3H, CH_3-CH_2-O-CO-C**H**$_2$-N) ; δ 2,83 (t, 2H, CH_3-CH_2-C**H**$_2$-S) ; δ 3,73 (s, 3H, -OC**H**$_3$) ; δ 7,09 (dd, J = 6 Hz,1H, H-5) ; δ 7,33 (d, J = 9 Hz, 1H, H-4) ; δ 7,41 (d, J = 2 Hz, 1H, H-7); δ 11,69 (s, 1H, -N**H**CO-).

Methyl (1-(oxiran-2-ylmethyl)-5-(propylthio)-benzimidazol-2-yl) carbamate 3i
IR (KBr) : v 2958, 1767, 1661,1442, 1336, 1219, 1079 cm^{-1}. ^1H NMR (300 MHz, DMSO-d6) δ 0,92 (t, 3H, C**H**$_3$-CH_2-CH_2-S) ; δ 1,52 (m, 2H, CH_3-C**H**$_2$-CH_2-S) ; δ 1,84 (m, 1H, O-C**H**-CH_2-N) ; δ 3,68 (m, 2H, O-CH-C**H**$_2$-N) ; δ 3,83 (t, 2H, CH_3-CH_2-C**H**$_2$-S) ; δ 3,73 (s, 3H, -OC**H**$_3$) ; δ 7,09 (dd, J = 6 Hz,1H, H-5) ; δ 7,33 (d, J = 9 Hz, 1H, H-4) ; δ 7,41 (d, J = 2 Hz, 1H, H-7); δ 11,69 (s, 1H, -N**H**CO-).

Méthyl (1-(2,3-dihydroxypropyl)-5-(propylthio)-benzimidazol-2-yl) carbamate 3j
IR (KBr) : v 2956, 1711, 1633,1588, 1443, 1325, 1224, 1095 cm^{-1}. ^1H NMR (300 MHz, DMSO-d6) δ 0,92 (t, 3H, C**H**$_3$-CH_2-CH_2-S) ; δ 1,52 (m, 2H, CH_3-C**H**$_2$-CH_2-S) ; δ 2,82 (s, 1H, CH_2OH-CHO**H**-CH_2-N) ; δ 2,84 (s, 1H, CH_2O**H**-CHOH-CH_2-N) ; δ 3,39 (s, 1H, CH_2OH-C**H**OH-CH_2-N) ; δ 3,74 (s, 2H, CH_2OH-CHOH-C**H**$_2$-N) ; δ 3,83 (t, 2H, CH_3-CH_2-C**H**$_2$-S) ; δ 3,73 (s, 3H, -OC**H**$_3$) ; δ 7,09 (dd, J = 6 Hz,1H, H-5) ; δ 7,33 (d, J = 9 Hz, 1H, H-4) ; δ 7,41 (d, J = 2 Hz, 1H, H-7); δ 11,69 (s, 1H, -N**H**CO-).

CONCLUSION

The search for new anti-hydatidosis is interesting for several reasons: limited therapeutic arsenal, the problem of bioavailability and the emergence of resistance. The new albendazole derivatives were synthesized and characterized by their spectral data.

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