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ORIGINAL PAPER

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Cytisine parameters measured in the 1.5 Tesla magnetic field

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ABSTRACT

Introduction. Cytisine, Cytisinum ($C_{11}H_{14}N_2O$), is an organic chemical compound. Cytisine is heterotricyclic compound that is the toxic principle in Laburnum seeds and is found in many members of the Fabaceae (legume, pea or bean) family.

Aim. The aim of the study is to measure the influence of water on the form of drug in the magnetic field 1.5 Tesla.

Material and methods. For this purpose, magnetic resonance imaging tests were performed to check the solubility of pure cytisine, Desmoxan tablets and Tabex capsules.

Results. From a pharmacological point of view, both Desmoxan tablets and Tabex capsules should exert the same effect on the human body, this is due to the identical content of the active substance, in this case cytisine (1.5 mg).

Conclusion. The differences in the results obtained may be related to additional excipients that contain medications, but it is believed that they should not have a negative impact on the action of the active substance.

Keywords. cytisine, desmoxan, magnetic resonance imaging, tabex

Introduction

Commonly used smoking cessation preparations are based on cytisine. Cytisinum ($C_{11}H_{14}N_2O$) is an organic chemical compound obtained on an industrial scale from the seeds of the Laburnum anagyroides shrub, which have toxic properties.[1-4] Because of its similarity to nicotine, cytisine is used as a substitute for nicotine to satisfy craving associated with an attempt to quit smoking.[5] Tabex and Desmoxan have the same active ingredient, but they differ in excipients. Tabex and Des-

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moxan are equivalent, that is, their action in the body is identical. Both contain the same active substance - cytisine, in an identical amount – 1.5 mg.[6-7] The differences only start at the stage of excipients and the form of the drug (capsule/tablet). In this case, the additive substances should not affect the drug's effect. In this work, we examined differences in parameters such as relaxation times for pure cytisine, Tabex tablets and Desmoxane capsules.[8-10]

Aim

The aim of the study is to measure the influence of water on the form of drug in the magnetic field 1.5 Tesla.

Material and methods

Measurements were made using Optima MR360 magnetic resonance imaging by General Electric Healthcare (Milwaukee, Wisconsin, USA) with a 1.5 Tesla field and a dedicated small flex transceiver. Basic sequences used for clinical trials were used. To compare popular pharmaceuticals, Desmoxan and Tabex tablets and pure cytisine were prepared (Figure 1). All MR scans were performed with Optima MR360 magnetic resonance from General Electric Healthcare (Milwaukee, Wisconsin, USA). The camera was supported in the SV23 software version. The prepared ependorf samples were placed in the MR tunnel and then a series of measurements was made to determine the relaxation times T1 and T2. The lung cancer cells in the vials were placed on the FLEX Small transceiver coil. To perform the measurements, the Fast Spin Echo (FSE) sequence was used with the following parameters: FOV field of view=10x10 [cm]; Matrix=320 x 224; NEX=2.0; Slice Thickness=1.0 [mm]; Spacing=0.5). TR time varied in the range of 48÷15000 [ms] (48, 50, 100, 150, 200, 300, 500, 1000, 1500, 2000, 3000, 5000, 10000, 15000 ms). TE time was 3 ms.

Fig. 1. Photo showing cytisine powder, Desmoxan capsule and Tabex tablet used for the study

Results

The Desmoxan caapsule was ground in 5 ml of water. Directly after placing the powder in water, the relaxation time T1 was measured. With the following snapping parameters, the repetition time was changed in the range TR=48 to 15,000, TE=3 ms (Figure 2).

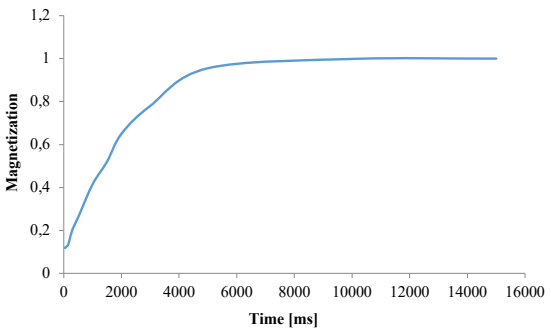

Fig. 2. T1 relaxation time curve for Desmoxan capsule induced in 5 ml H_2O

In the next step, after 24 hours, a series of measurements were again made to determine the relaxation time T1 (the tablet was lying in water all the time), the value of T1=1330 ms was obtained (Figure 3).

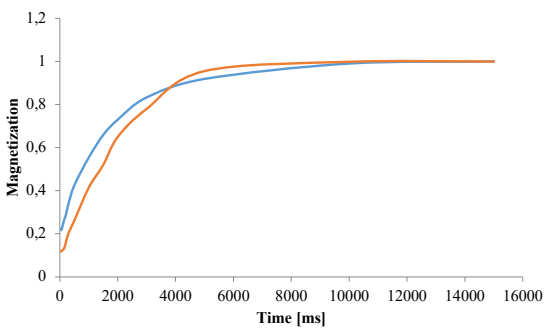

Fig. 3. T1 relaxation curves for the Desmoxan capsule induced in 5 ml H_2O and the same capsule after 24h. The curve is marked in orange on the chart after 24 hours

In the next stage, after 72 hours, the measurements were repeated, and the relaxation time T1 was again determined, where its value strongly approached the water value and injected T1=3070 ms, which may indicate the dissolution of the tablet (Figure 4).

In the graph, the curve is marked orange after 24 hours, while the curve is marked green after 72 hours. On the graph, the curve is marked orange after 24 hours, while the curve is marked green after 72 hours. The results of relaxation times are shown in the table below (Table 1).

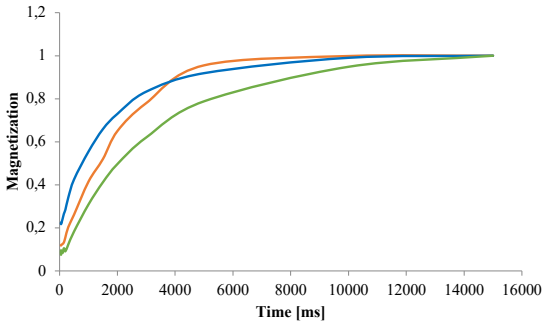

Fig. 4. T1 relaxation time curves for Desmoxan capsule induced in 5 ml H_2O and the same capsule after 24h and 72h

Table 1. T1 relaxation times

Sample	Desmoxan capsule	Desmoxan capsule after 24h	Desmoxan capsule tablet after 72h
T_1 [ms]	1946	1330	3070

In the next step of the test, the oil solubility test of Desmoxan (5ml) was performed. The relaxation time T1 was determined which was T1=205 ms, then the series of measurements was repeated after 16h and the relaxation time was again determined which was T1=158 ms (Figure 5).

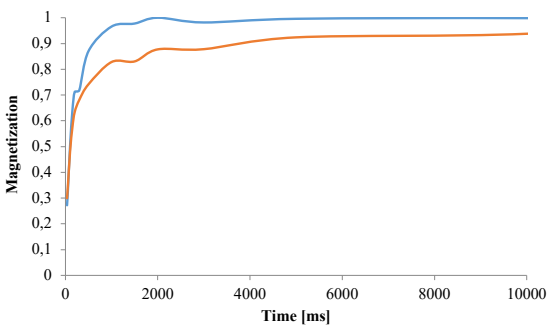

Fig. 5. T1 relaxation time curves for Desmoxan capsule induced in 5 ml oil and the same capsule after 16h

On the graph, the relaxation time curve marked immediately after placing the tablet into the oil is marked in blue, while the curve is marked orange after 16h. The results of relaxation times are shown in the table below (Table 2).

Table 2. T1 relaxation time

Sample	Desmoxan capsule in oil	Desmoxan capsule after 24h in oil
T_1 [ms]	205	158

To compare the results, scans of oil, water and vinegar were performed without the addition of drugs. The following relaxation time results were obtained: T1 oil=177 ms, T1 vinegar=1894 ms, T1 water=3200 ms.

The table 3 shows the results of T1 relaxation times for tablets with the addition of various solvents.

Table 3. T1 relaxation times for tablets with the addition of various solvents

Sample	Cytisine	Desmoxan	Tabex
+5 ml vinegar	648 ms	573 ms	1107 ms
+5 ml oil	171ms	169 ms	170 ms
+5 ml water	984 ms	1066 ms	1498 ms

The table 4 shows the results of T2 relaxation times for tablets with the addition of various solvents.

Table 4. T2 relaxation times for tablets with the addition of various solvents

Sample	Cytisine	Desmoxan	Tabex
+5 ml vinegar	86	34	37
+5 ml oil	64	63	65
+5 ml water	90	38	47

Discussion

Discovery of cytisine properties provides an opportunity for further interrogation of the physiological roles of nicotinic receptor.[11-13] Our observation during this experiment was that during 72 h in water, all form of discussed here drugs (Cytisine powder, Desmoxan capsules and Tabex tablets) were dissolved in water and both relaxation time of solutions decresed due to higher drug concentration in soluble form.

The addition of various solvent to cytisine shows decrese in T1 and T2 values when compared to cytisine dissolved in pure water. Desmoxan capsules and Tabex tablets showed similar behaviour in solubility. The amount and solubility in different media may induce changes in drug efficacy.[14-15] In our study we observed that only pure water was good media to analyze solubility of discussed drugs. The density of media in variable solvents is an important factor to discuss during a new drug preparations.[16-21]

Conclusion

The diffrences between pure Cytisine, Tabex and Desmoxan are base on chemical composition of tablets. Desmoxan contein T lactose monohydrate, microcrystalline cellulose, talk and magnesium stearate. Tablex contein microcrystalline cellulose, corn starch, colloidal anhydrous silica and magnesium stearate. The results of Tabex and Desmoxan solubility are visible where compared to pure cytisine powder.

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