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INTRODUCTION

Depression affects over 350 million people worldwide and is associated with high mortality and morbidity.

The aim of this study is to assess the effect of the association of two antidepressants - hyperforin, main constituent of *Hypericum perforatum* (St John's Wort) and sertraline.

Hyperforin acts as a natural inhibitor of catecholamines reuptake. Disruptions in the activity of these neurotransmitters are reported as the underlying cause of depression. Sertraline is a potent and specific inhibitor of neuronal serotonin reuptake, which results in the potentiation of the effects of this neurotransmitter.

METHODS

Stage 1. Induction of depression

- 8 groups of 10 animals.
- 0,1 mg/kg reserpine p.o. daily, 21 days.
- behavioural assessment using tail-suspension test (TST), baseline and after 21 days of administration (6 minutes/animal/testing session)
- locomotor activity assessment using Ugo Basile actometer after 21 days of administration (5 minutes/animal). This test, coupled with TST, allows to separate the locomotor stimulant doses from antidepressant doses.

Stage 2. Assessment of antidepressant effect for several *Hyperici* extracts, alone or in association with sertraline

- animal selection based on the results of TST (undertaken after 21 days of reserpine administration) and distribution in 8 homogenous groups.
- daily administration:
 - group 1 (control): water 0.1 ml/10 g, p.o.
 - group 2 - hyperforin, 15 mg/kg, suspension 0.15%, p.o. (Faculty of Pharmacy Chisinau, Moldova)
 - group 3 - dried extract of *Hyperici herba* (E1) (250 mg extract corresponds to 0.5 mg total hypericin) 300 mg/kg, suspension 3%, p.o.
 - group 4 - *Hyperici herba* extract (E2) (obtained by the Department of Botany, Faculty of Pharmacy, Bucharest) 300 mg/kg, suspension 3%, p.o.
 - group 5 - sertraline 25 mg/kg, suspension 0.25%, p.o.
 - group 6 - hyperforin 15 mg/kg, suspension 0.3% + sertraline 25 mg/kg, suspension 0.5% p.o (A1).
 - group 7 - dried extract of *Hyperici herba* (250 mg extract corresponds to 0.5 mg total hypericin) 300 mg/kg, suspension 6% + sertraline 25 mg/kg, suspension 0.5% p.o (A2).
 - group 8 - *Hyperici herba* extract (Department of Botany, Faculty of Pharmacy, Bucharest), suspension 6% + sertraline 25 mg/kg, suspension 0.5% p.o (A3).
- assessment of TST and motor activity after 1, 7 and 15 days of daily administrations. Testing was performed after one hour from administration of the substances.

RESULTS

The statistical interpretation of the results was made by using ANOVA (soft GraphPad Prism 5). ANOVA was applied for populations with normal distribution. The type of distribution was assessed using d'Agostino & Pearson test. Posttest Bonferroni was applied when ANOVA revealed statistical significance ($p < 0.05$), to compare groups two by two.

1. Induction of depression

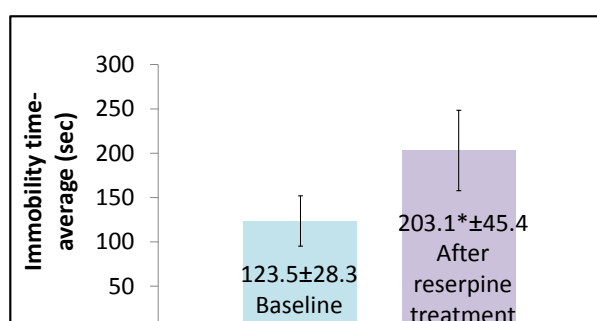


Fig. 1 - Immobility time (average ± DS) before and after reserpine administration

Table 1. Animal distribution into homogenous groups based on TST values

Group	1	2	3	4	5	6	7	8
Average	202.1	201.4	200.4	201.2	201.5	200.9	201.4	200.6 ±
TST ± DS	± 41.2	± 56.5	± 63.4	± 55.8	± 42.6	± 26.9	± 60.5	54.8
ANOVA	NS (P > 0.05)							

2. Assessment of antidepressant effect of *Hyperici* extracts and their associations with sertraline

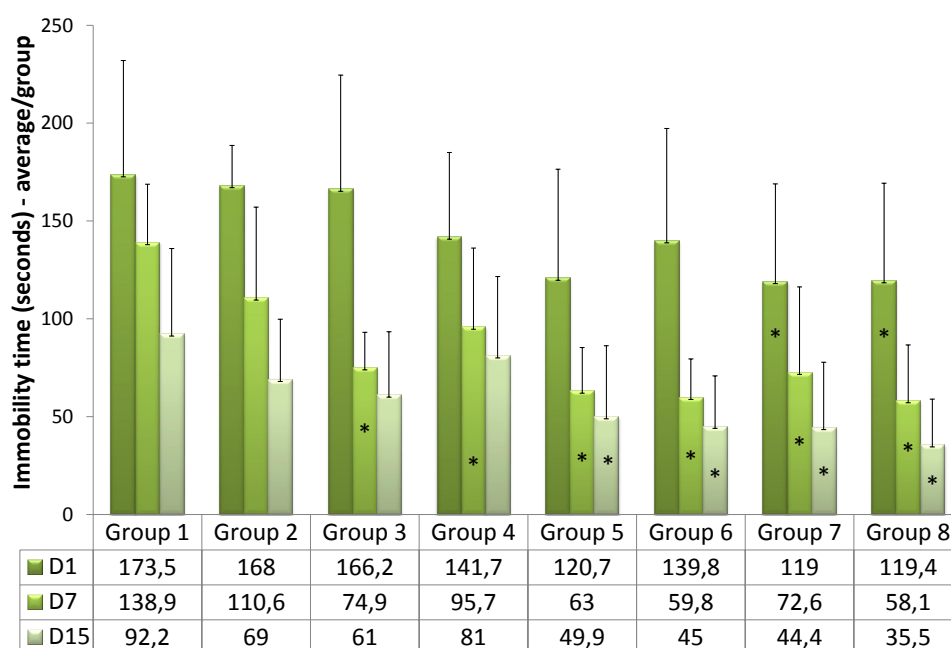


Fig. 2 - Immobility time following 1 day, 7 days and 15 days of administration *- variation vs. Control group (group 1) has statistical significance ($p < 0.05$)

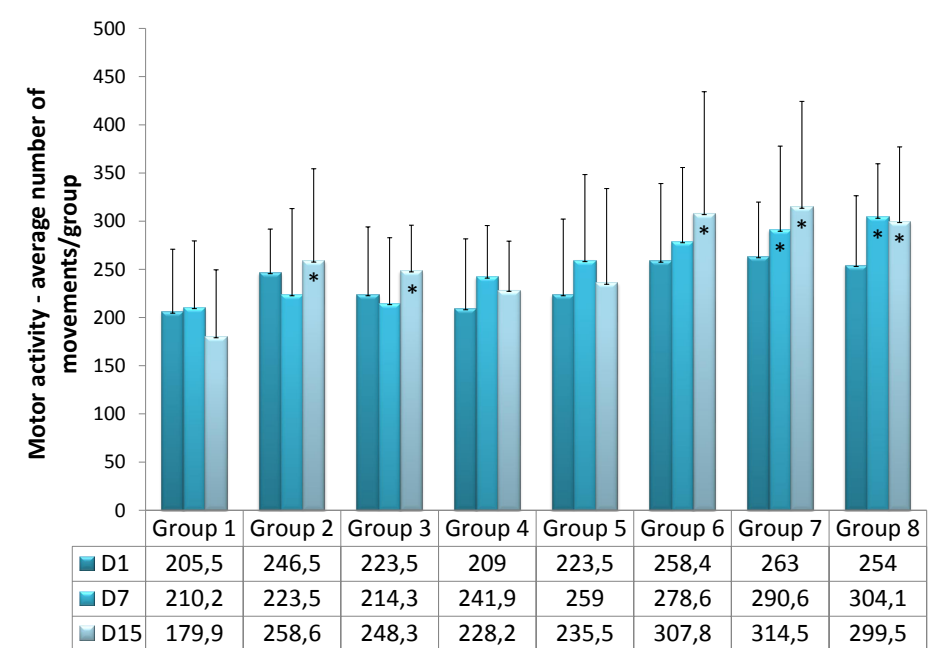


Fig. 3 - Motor activity following 1 day, 7 days and 15 days of administration *- variation vs. Control group (group 1) has statistical significance ($p < 0.05$)

Table 2. Percent variation of immobility time (IT) and horizontal motor activity (HMA) for groups 6, 7, 8 vs. group 5 (sertraline)

	1 day of administration	7 days of administration	15 days of administration
%variation IT			
Group 6	15.82	-5.07	-9.82
Group 7	-1.41	15.24	-11.02
Group 8	-1.08	-7.77	-28.85
%variation HMA			
Group 6	15.62	7.57	30.70
Group 7	17.67	12.20	33.55
Group 8	13.65	17.41	27.18

CONCLUSIONS

All three tested *Hyperici* products showed an antidepressant effect after 15 days of administration. There are no significant differences between different extracts regarding the antidepressant efficacy.

All three extracts potentiate the antidepressant effect of sertraline and could be used in therapeutics. We must mention that there our results suggest that using the associations may increase the risk of inducing motor agitation.

ACKNOWLEDGEMENTS

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