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**Effects of Single and Long Term Use of
Polyphenols on Absorption and Tissues
Distribution of Drugs (metformin and atenolol)
and Trace Elements (zinc, copper and iron) in Rats**

A Thesis

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Abstract

Background and Objective

In recent years, there has been a remarkable progress in understanding the pharmacological and toxicological impact of polyphenols and the possibility of pharmacokinetic interaction of polyphenols-drugs or trace elements interactions that may have undesirable therapeutic outcomes or may be desirable to reach specific targets. Accordingly, the present study was designed to evaluate both long-term and single dose effect of polyphenols(silibinin, epigallocatechin, quercetin and rutin) on the absorption and tissue distribution of drugs (metformin and atenolol) and trace elements (zinc, copper and iron) after single oral doses of each.

Methods

In long term study, thirty rats were used, allocated into 5 groups and treated as follow: 1st group treated with olive oil and served as control; the other 4 groups were treated with either silibinin(100mg/kg), EGCG(25mg/kg), quercetin(50mg/kg) or rutin(500mg/kg), administered orally as oily solutions for 30 days. At day 31, a solution contains sulphate salts of zinc(60mg/kg), copper(60mg/kg) and iron(60mg/Kg) was administered orally; meanwhile, a solution contains metformin(300mg/kg) and then atenolol(50mg/kg) were administered orally by gavage tube. In short term study, regarding polyphenols the same design was followed, in other hand the same doses of the drugs and trace elements were administered as in long term study, where single daily doses were orally administered; the effect was compared with that reported in vehicle treated control group. The animals were sacrificed after 3 hours of metformin dose and blood samples, tissues of brain, kidney and liver were obtained for evaluation of the plasma and tissues

concentrations of metformin, atenolol, Zn, Cu and Fe using HPLC and atomic absorption spectrometry.

Results

In long term study the results showed that all four polyphenols groups increased both serum and tissue levels of metformin but they had no effect on atenolol level compared with control group. Furthermore, serum and tissue concentrations of Zn, Cu and Fe were increased significantly compared with control. Meanwhile, in the single dose study, all four polyphenols groups decrease serum and tissues concentration of trace elements compared with control, but led to increase serum and tissues levels of metformin without any significant effect on atenolol level.

Conclusion

Both single doses and long-term use of supraphysiological doses of silibinin, EGCG, quercetin and rutin increased absorption and tissues availability of metformin but not atenolol, more ever opposite results in this study were revealed that long term use of polyphenols increased serum, brain, liver and kidney levels of Zn, Cu and Fe, while single dose study reveal a significant decrease in this respect.