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Research paper

Evaluating the anticoagulant effect of medicinal plants *in vitro* by cheminformatics methods

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ABSTRACT

Introduction: This study was designed to evaluate the anticoagulant effect of some medicinal plants using cheminformatics methods.
Material and methods: Databases such as PubMed and Google Scholar were searched to collect information regarding anticoagulant compounds and plants showing this bioactivity. According to the identified anticoagulant compounds, cheminformatics methods were set to find all similar compounds by using the PubChem Structure Search engine. Then, with the help of the identified similar compounds, 15 medicinal plants native to Iran containing at least one of the similar compounds were prepared and extracted in ethanol and the sample extracts were dissolved in DMSO. Three concentrations 1, 10 and 100 μg/ml of extracts were prepared to investigate their anticoagulant effect. Finally, the anticoagulant effect of the selected medicinal plants was evaluated by *in vitro* PT and APTT assays.
Results: The extracts of 5 plants, including *Ocimum basilicum, Rosa persica*, *Trigonella foenum*, *Solanum nigrum* and *Cubeba officinalis* at a concentration of 100 μg/ml showed a significant anticoagulant effect on APTT test in comparison with the negative control.
Conclusion: In this study, the anticoagulant effect was identified as a significant property of five medicinal plants. These plants can be regarded as likely candidates for prevention and treatment of complications in individuals with high risk of stroke or ischemia. Also, we suggest that these plants should be cautiously consumed with anticoagulant drugs (*e.g.* heparin) due to a risk of hemorrhage and increase in the effect of anticoagulant drugs.

1. Introduction

Blood coagulation is a homeostatic mechanism by which the body arrests bleeding or hemorrhage caused as a result of damage or injury to blood vessels. Diseases like hemophilia, which is caused by shortages or lack of some coagulation factors, can be very harmful and in some cases lethal. In contrast, unnecessary coagulation and aberrant blood clots can stop normal blood flow and prevent the arrival of nutrients and oxygen to the adjacent tissues. This process can lead to the death of cells and tissues, thus causing cardiovascular diseases (Key et al., 2009). Cardiovascular diseases are among the most prevalent causes of death in recent years. In 2012 these diseases plus stroke ranked first and second in terms of the number of deaths in the world (WHO, April, 2015). The most important of these disorders are heart attacks and stroke caused by misplaced clots in the blood vessels, often as a result of lack of movement, poor nutrition, ageing and smoking in individuals. It is widely acknowledged that nutritional factors and proper physical activity, together with compliance with appropriate medication play an important role in the prevention and treatment of these complications (Goldstein et al., 2001).

Most pharmaceutical drugs have side effects that may be experienced alongside their therapeutic actions (Kuhn et al., 2010); for example, warfarin, a commonly used anticoagulant drug, demonstrates side effects that include bruising, bleeding gums, red or dark brown urine, red or black bowel motions, nosebleeds, haemoptysis, dyspnoea and dysphagia, heavier than usual menstrual periods, excessive wound bleeding, dark or blood-

Abbrevations: PT, Prothrombin Time; APTT, Activated Partial Thromboplastin Time; μg/ml, micrograms per milliliters; DMSO, dimethyl sulfoxide.

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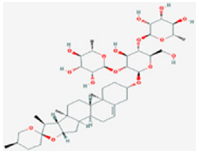
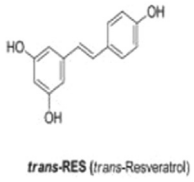
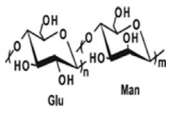
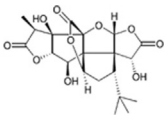
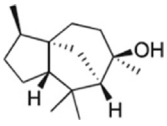
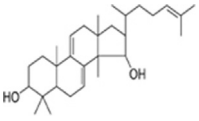
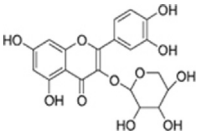
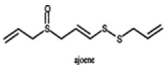
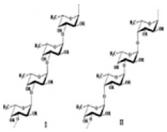
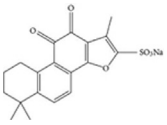
Table 1
The literature study results for anticoagulant compounds and substances.

No.	Compound	Source	Chemical Structure	CVDHD ID	Reference
1	Dioscin	Plant		CVDHD003160	Xu et al. (2012)
2	Resveratrol	Plant		CVDHD027151	Delmas et al. (2005)
3	Konjac glucomannan	Plant		–	Delmas et al. (2005)
4	Ginkgolide B	Plant		CVDHD002218	Singh et al. (2013)
5	Cedrol	Plant		CVDHD022603	Singh et al. (2013)
6	Polycarpol	Plant		–	Singh et al. (2013)
7	Quercitrin	Plant		CVDHD007261	Singh et al. (2013)
8	Ajoene	Plant		CVDHD023677	Flamini (2003)
9	Fucoidan	Seaweed		–	Vo and Kim (2013)
10	Tanshinone IIA	Plant		CVDHD009052	Shang et al. (2012)