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Open access in Silico Tools to predict the ADMET profiling for Substances of Bioactive compounds of Garlic (Allium sativum L.)

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***Abstract*—** in this work, we have investigated the main bioactive components of garlic through a bioinformatics approach. Particular attention, we focused on the role of two active garlic compounds: S-allyl cysteine (SAC), S-allyl mercapto cysteine (SAMC), respectively. We investigated their biological and chemical property by different in Silico Tools databases, as PASS database, SwissADME, PreADMET and pkCSM. They were employed to determine their ADMET properties (metabolism, distribution, excretion, absorption, and toxicity).

Keywords— PASS Online , ADMET, S-allylcysteine (SAC), S-allylmercaptocysteine (SAMC)

I. INTRODUCTION

Garlic (Allium sativum L.) belonging to the Liliacee family, it is a species in the onion genus Allium. The knowledge and use of this plant has ancient origins. It has been demonstrated to exhibit potentially beneficial for cancer prevention.

Several studies have demonstrated its functions such as anti-inflammatory, antibacterial, and antiviral, antioxidant, cardiovascular protective and anticancer property [1, 2].
The consumption of garlic in the diet provides strong protection against cancer risk [2].

In Literature, we there are some papers, where it was demonstrated decreased rates stomach cancer associated with garlic intake [3, 4, 5].
We have investigated the main bioactive components of garlic through a bioinformatics approach. [6, 7].

This paper encompasses the fundamental functions of open access in Silico prediction tools, as PASS database (Prediction of Activity Spectra for Substances) that it estimates the probable biological activity profiles for compounds [8,9] .

Garlic contains several active sulfur compounds for instance aliin, allicin, ajoene, allylpropl, diallyl, trisulfide, s-allylcysteine, vinyldithiines, S-allylmercaptocystein. (See below figure 1).

The present work investigated two different sulphide compounds of garlic, by Computation approach, for their anti-tumor properties, as (SAC) and (SAMC) rispectively. (See below figure 2).

Several open-access databases are available to date, like (PASS database, available bioinformatics tool, SwissADME, PreADMET pkCSM respectively). [6, 7, 8, 9].

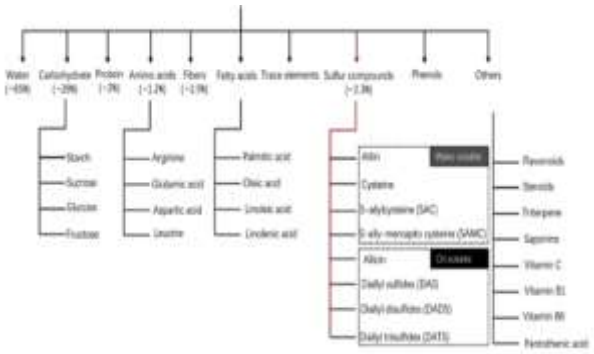

Figure 1. Major classification of the bioactive constituents in garlic. Generally, garlic bulb contains approximately 65 % water, 28 % carbohydrates (mainly fructans), 2 % protein (mainly alliin), 1.2 % free amino acids (mainly arginine), 1.5 % fiber, and 2.3 % organosulfur compounds. Figure reproduced from Reference [2].

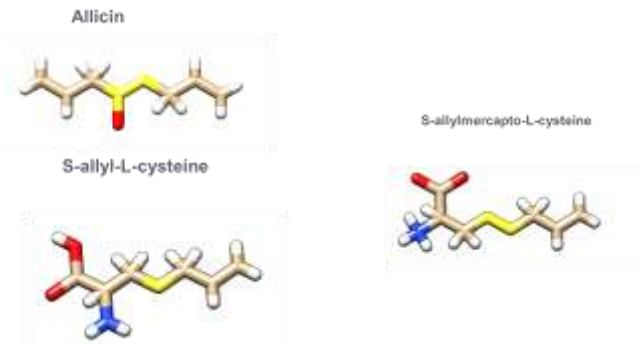

Figure 2. Bioactive constituents in garlic Sulphur compounds: Allicin, SAC and SAMC respectively.

II. Related Work

The main goal of this paper is intended to Pharmacokinetic properties by several servers, of S-allyl cysteine (SAC) and S-allyl-mercapto cysteine (SAMC) for their anti-inflammatory, antibacterial, and antiviral, antioxidant, cardiovascular protective, and anticancer properties. [10,11,12,13,14,15,16,17,18,19,20].

In figure 3 we report 3D Chemical structures of studied bioactive constituents in garlic.
They were download from PubChem (https://pubchem.ncbi.nlm.nih.gov/) and reproduced by Discovery Studio Biovia Software [21].

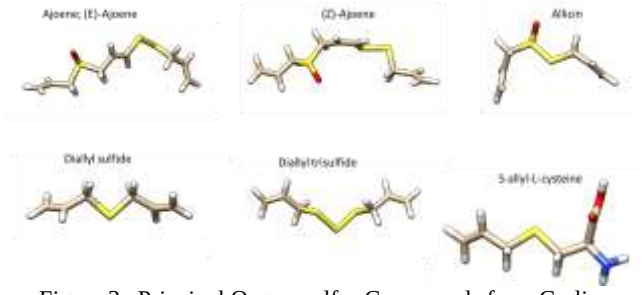

Figure 3. Principal Organosulfur Compounds from Garlic.

III. Methodology

- PASS (http://www.way2drug.com/passonline/)
- PreADMET (https://preadmet.bmdrc.kr/)
- pkCSM (http://biosig.unimelb.edu.au/pkcsm/) were employed to determine the ADMET (metabolism, distribution, excretion, absorption, and toxicity) attributes of target molecules.
- SwissADME (http://www.swissadme.ch/index.php) [7]

IV. Results and Discussion

PASS database (Prediction of Activity Spectra for Substances)
PASS Online predicts different kinds of biological activity, including pharmacological effects, mechanisms of action. [9, 22]
It is used by medicinal chemists and pharmacologists for several years (Lagunin et al., 2000) [23].

Results come as two different probabilities: Pa (probability to be active) and Pi (probability to be inactive).

In general, the more types of activity that are predicted as probabilities for a compound, the more likely it is that a useful pharmacological action will be found there.

For each compound from available set of samples the following value can be calculated [9]:

$$P = 1/n \sum Pa/(Pa + Pi) \qquad (1)$$

In Figure 4, we report chemical-physical properties of Principal Organosulfur Compounds, S-allylcysteine (SAC) and S-allylmercaptocysteine (SAMC) investigated by Pass Online Server, that it estimates the probable biological activity profiles for compounds.

Indeed, SAMC and SAC demonstrated to a suppressive agents against several tumours. [10,11,12,13,14,15,16,17,18,19,20].
From our results of Prediction of Activity Spectra and ADME parameters, S-allylcysteine and S-allylmercapto-cysteine have a high value of 0.96-0.98 Pa (probability to be active) in human flavin-containing monooxygenase 3 (FMO3) and it has impact on enzyme activity, drug metabolism and disease[27, 28]. Several further studies are underway on the molecules studied in the present paper. Recently we have published work, based on the role of SAMC intercalated within the nanomaterial in Layered Double Hydroxides, ZnAl-LDH, which demonstrates that the LDH-SAMC complex showed the improved efficacy of the action of SAMC in reducing the invasive capacity of a human hepatoma cell line [29].

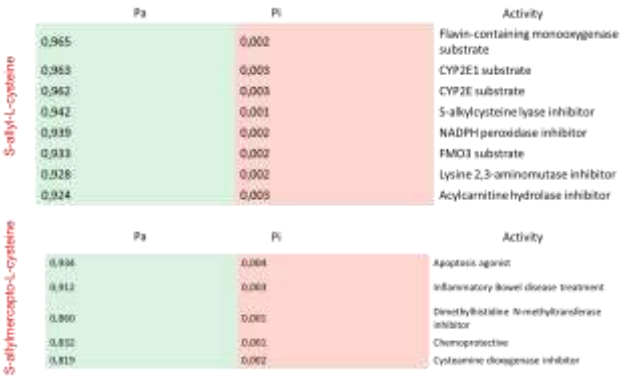

Figure 4. Prediction of Activity Spectra for Substances of Principal Organosulfur Compounds, as S-allylcysteine (SAC) and S-allylmercaptocysteine (SAMC).

In Silico Organosulfur Compounds analysis and ADMET profiling
The available bioinformatics tool SwissADME (http://www.swissadme.ch/index.php) was used for finding drug-likeness attributes [23].
Lipinski's rule of five [6] was used to analyze the properties such as; hydrogen bond donor (HBD), hydrogen bond acceptor (HBA), molecular weight (MW), and lipophilicity (log P).

SwissADME (http://www.swissadme.ch/index.php)

This website allows you to compute physicochemical descriptors as well as to predict ADME parameters, pharmacokinetic properties such as hydrogen bond donor (HBD), hydrogen bond acceptor (HBA), molecular weight (MW), and lipophilicity (log P) [6,23] .

Figure 5. Physicochemical descriptor, ADME parameters, pharmacokinetic properties, drug like nature and medicinal chemistry friendliness of S-allylcysteine (SAC) predicted by SwissADME Database.

Figure 6. Physicochemical descriptors, ADME parameters, pharmacokinetic properties, drug like nature and medicinal chemistry friendliness of S-allylmercaptocysteine (SAMC) predicted by SwissADME Database.

PreADMET (https://preadmet.bmdrc.kr/)

PreADMET is a web-based application for predicting ADME data and building drug-like library using in Silico method. [24, 25].

In figure 7 we report ADMET parameters of SAC and SAMC, respectively, predicted by PreADMET.

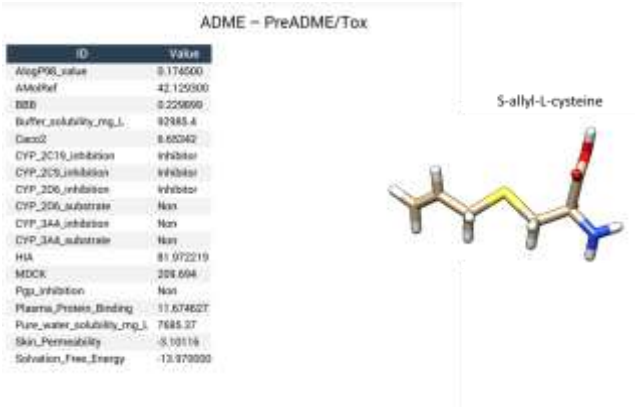

Figure 7. ADMET (metabolism, distribution, excretion, absorption, and toxicity) attributes of S-allylcysteine (SAC) predicted by PreADMET.

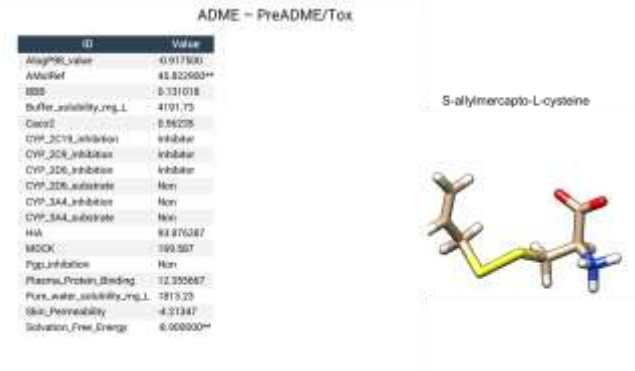

Figure 8. ADMET (metabolism, distribution, excretion, absorption, and toxicity) attributes of S-allylcysteine (SAC) predicted by PreADMET (https://preadmet.bmdrc.kr/).

pkCSM (http://biosig.unimelb.edu.au/pkcsm/)

In figure 8, we report ADMET parameters of SAC and SAMC, rispectively, predicted by PreADMET.[24,25]:

pkCSM have predictive models for different pharmacokinetic classes: Absorption, Distribution, Metabolism, Excretion and Toxicity [26].

In figure 9, 10 we report Prediction of pharmacokinetic properties: ADMET parameters attributes to SAC, SAMC predicted by pkCSM, respectively. [26]

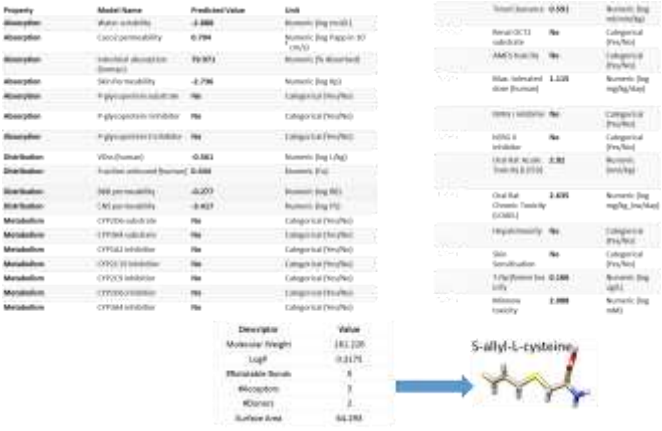

Figure 9. Prediction of pharmacokinetic properties: ADMET (metabolism, distribution, excretion, absorption, and toxicity) attributes of S-allylcysteine (SAC) predicted by pkCSM.

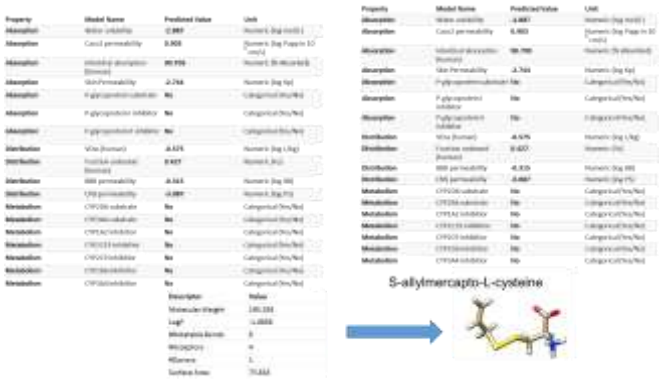

Figure 10. Prediction of pharmacokinetic properties: ADMET (metabolism, distribution, excretion, absorption, and toxicity) attributes of S-allyl-mercapto-L-Cysteine (SAMC) predicted by pkCSM.

V. CONCLUSION AND FUTURE SCOPE

We focus on the role of bioactive compounds in garlic, as S-allyl cysteine (SAC) and S-allyl- mercapto-L- cysteine (SAMC). Several in vitro studies are ongoing of these anticancer compounds in garlic.

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