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Issue Article

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MOLECULAR DOCKING STUDIES OF Cu(II), Zn(II), Co(II), Ni(II) COMPLEXES WITH ABSCISIC ACID AND MONOETHANOLAMINE

Abstract: *The protein-ligand binding studies of [Me(ABA)$_2$(MEA)] and [Me(ABA)$_2$(MEA)$_2$] (here, Me= Cu(II), Zn(II), Co(II), Ni(II); ABA= abscisic acid; MEA= monoethanolamine) complexes with AtTIR1 protein (PDB ID: 2P1O) have been carried out using CB-Dock2 server. The binding energies of coordination compounds to the target 2P1O protein are significantly improved compared to the ABA or MEA molecule. Zinc and copper coordination compounds with two ABA molecules and one MEA molecule interact with the protein more strongly than other compounds, forming an H-bond with the following amino acid residues ARG9, TYR298, ARG344 and ARG403.*

Key words: *Abscisic acid, monoethanolamine 2P1O, docking studies, PDB database.*

Language: *English*

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Introduction

Phytohormones regulate the protective responses of plants against both biotic and abiotic stresses by means of synergistic or antagonistic actions referred to as signaling crosstalk. Plants adapt to or tolerate stress through production of specific hormones that are produced at very low concentrations. One of the classical and well-studied phytohormones is abscisic acid (ABA), the importance of which is highlighted by its various roles in development (such as seed dormancy, germination, and floral induction) and stress responses (such as drought, salinity, and pathogen infection) [1-5]. The molecular structure of ABA consists of a cyclohexene ring with a monomethyl group, a dimethyl group, a ketone group, a hydroxyl group and a hydrocarbon side chain conjugated to the carboxylic acid group (Fig. 1).

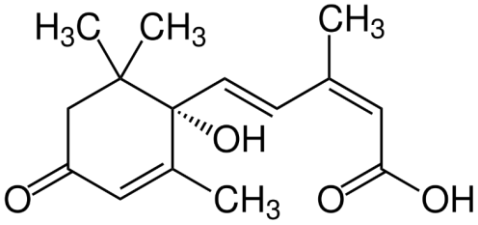


Fig. 1. Structure of ABA

Under stressful environmental conditions such as water shortage, high salinity and temperature extremes, the ABA content in plants rises significantly, stimulating stress-tolerance effects that help plants adapt and survive under these adverse conditions (Fig. 2.) [6].

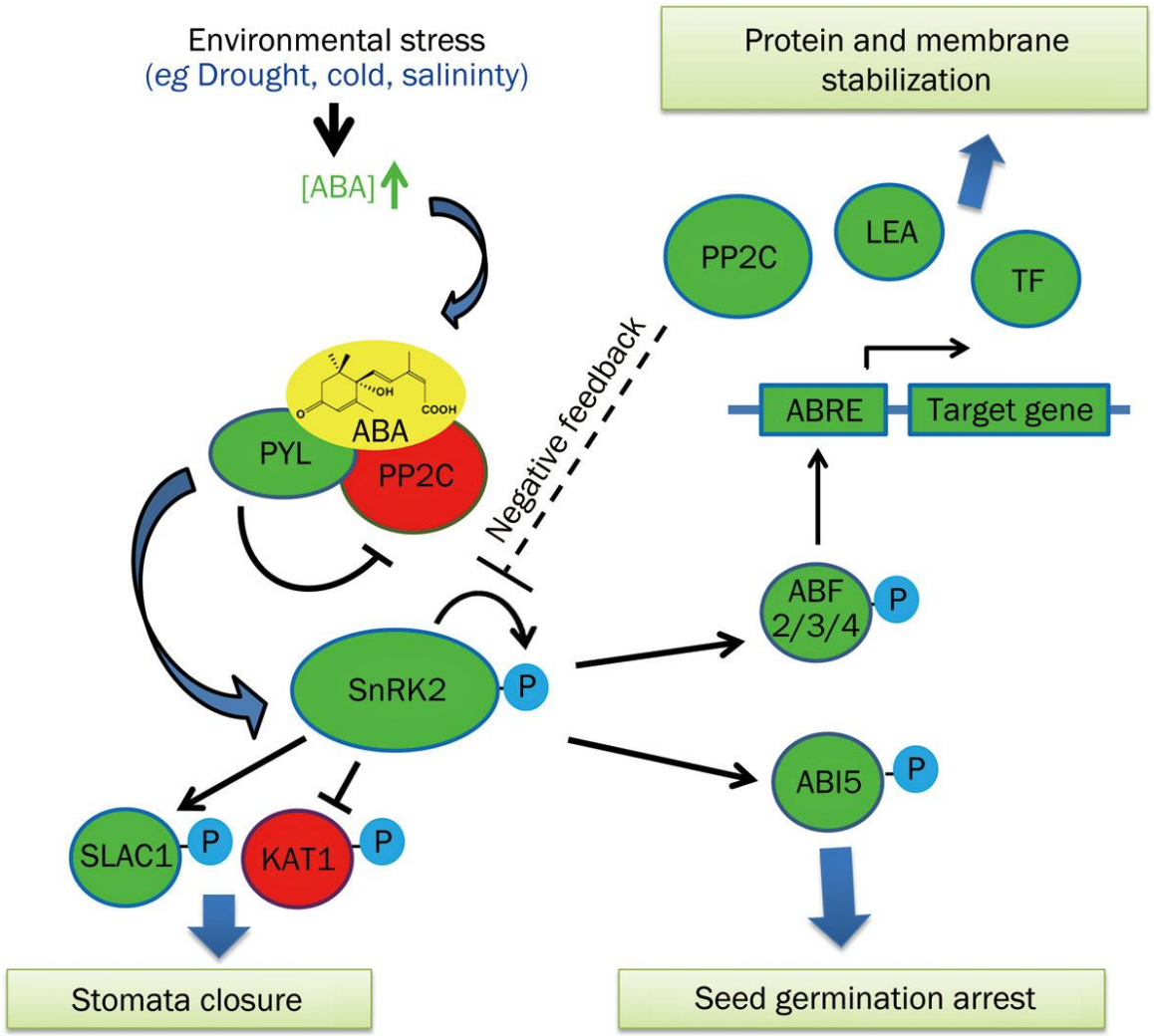


Fig. 2. ABA-mediated abiotic stress response

Under drought or osmotic stress conditions, ABA promotes stomatal closure, which prevents water loss through transpiration, and the accumulation of osmocompatible solutes to retain water [7,8]. The role of ABA as a negative regulator of plant growth has also been long established [9]. The activity of ABA in the induction and maintenance of seed dormancy is attributed to its potent effects on the inhibition of seed germination [10]. The inhibitory effects of ABA on germination and growth help plants withstand these stressful conditions and germinate only when the conditions are favorable for growth.

Moreover, ABA is not only involved in stress response, but also in plant growth by regulating the gene responsible for certain physiological processes ranging from stomatal opening to storage of proteins [11]. The receptors involved in ABA signaling were first discovered in Arabidopsis and it involves three major components- receptor PYR/PYL/RCAR (PYL-Pyrabactin resistance 1) protein family, positive regulator class III SNF-1-related protein kinase 2 (SnRK2) and negative regulator type 2C protein phosphatase (PP2C) [12]. PYR proteins are responsible for carrying out proper ABA signal transduction in Arabidopsis [13] and PP2Cs function as negative regulators in ABA-dependent pathways [14]. In this work, we theoretically studied the binding energy of metal complexes based on ABA and monoethanolamine (MEA) with proteins.

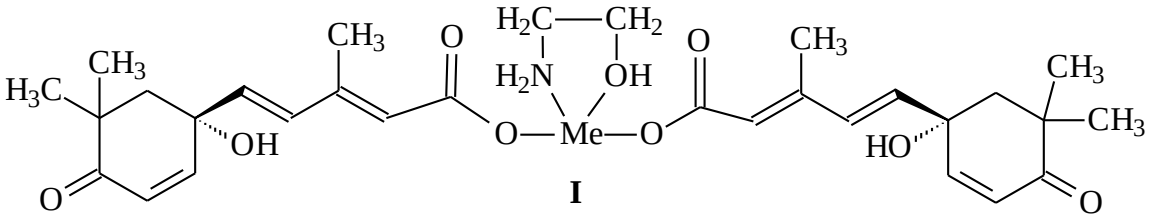
Materials and methods

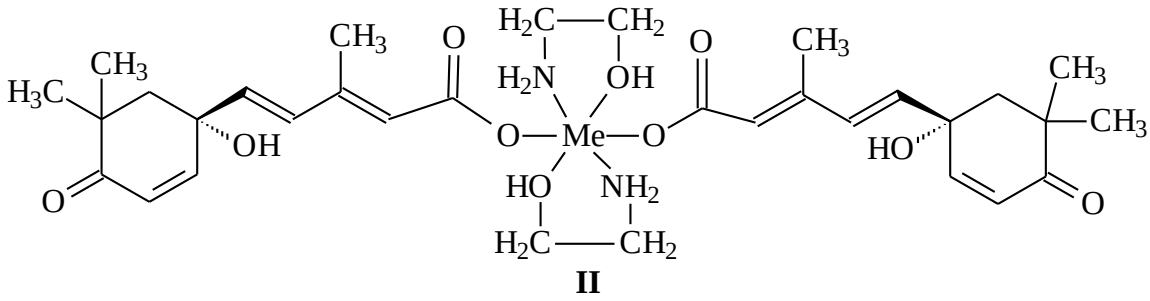
The geometry of ABA, MEA, and hypothetical coordination compounds was constructed using the Avogado software package [15]. Molecular docking studies have been carried out by CB-Dock2 server [16]. The target protein of AtTIR1 (PDB ID: 2P1O) was downloaded from PDB database [17].

Results and discussion

ABA is a plant hormone that regulates numerous aspects of plant growth, development, and stress responses. Molecular docking studies with the CB-Dock2 server were carried out to find new plant regulators. Hypothetical structures (Scheme 1) of coordination compounds based on MEA, ABA and metal ions (Cu(II), Zn(II), Co(II), Ni(II)) are constructed taking into account the fact that coordination compounds are more active than ligand molecules.

The protein-ligand binding of $[Me(ABA)_2(MEA)]$ and $[Me(ABA)_2(MEA)_2]$ (here, Me= Cu(II), Zn(II), Co(II), Ni(II); ABA= abscisic acid; MEA= monoethanolamine) complexes with AtTIR1 protein (PDB ID: 2P1O) was studied on the CB-Dock server. The results obtained are presented in table 1. It was found that the binding energy of ABA molecule with 2R1O protein is -5.7 kcal/mol and it forms H-bond only with GLU141 and ASP167 amino acid residues (Fig. 3). It was found that significant changes in binding energies occur in metal complexes. For example, the binding energy of the $[Zn(ABA)_2(MEA)]$ complex with metallic zinc is -9.7 kcal/mol, and it was found that the resulting complex has an H-bond with amino acid residues ARG9, TYR298 , ARG344 and ARG403 (Fig. 4).





Scheme 1. The structure of hypothetic coordination compounds. Me – Cu(II), Zn(II), Co(II), Ni(II).

Table 1. Binding energies of hypothetic structures to 2P1O

Compounds	Binding energy, kcal/mol	Contact residues with H-bond
$[Cu(ABA)_2(MEA)_1]$	-7.5	ARG9, TYR11, ASP167
$[Zn(ABA)_2(MEA)_1]$	-9.7	ARG9, TYR298, ARG344, ARG403
$[Co(ABA)_2(MEA)_1]$	-9.3	ARG9, TYR298, ARG344
$[Ni(ABA)_2(MEA)_1]$	-9.7	ARG9, TYR298, ARG344, ARG403
$[Cu(ABA)_2(MEA)_2]$	-7.1	-
$[Zn(ABA)_2(MEA)_2]$	-9.9	ARG9, ASP81, ARG344, ARG403
$[Co(ABA)_2(MEA)_2]$	-9.6	ARG9, ASN83, TYR298
$[Ni(ABA)_2(MEA)_2]$	-8.2	ARG9, ASN83
ABA	-5.7	GLU141, ASP167
MEA	-2.7	CYS140, GLU141

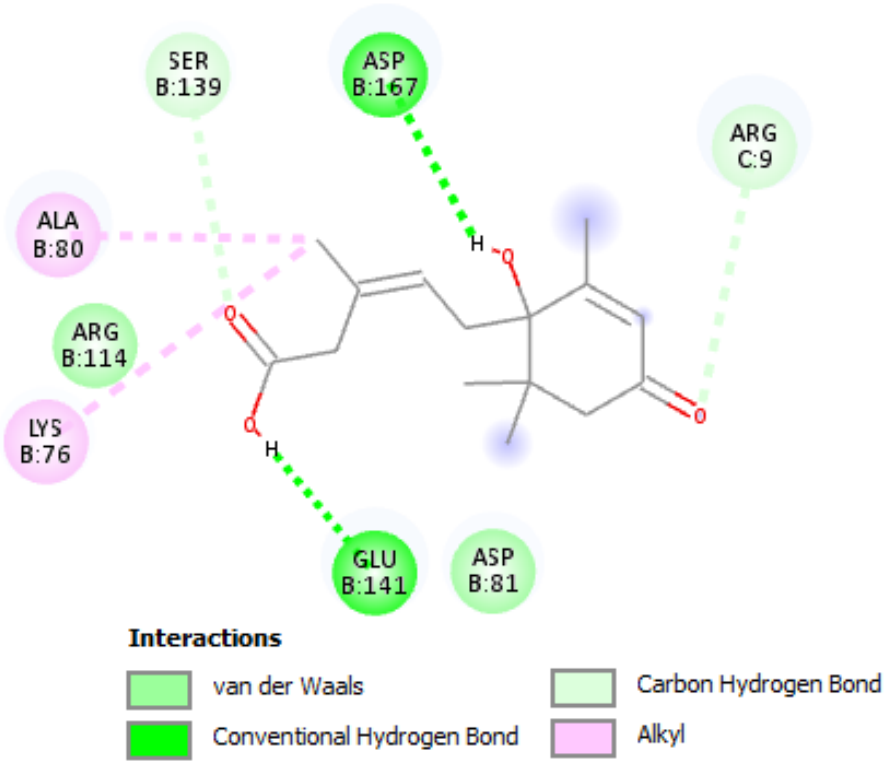


Fig. 3. Contact residues in the active site of the protein in 2P1O-ABA complex docked by CB-Dock2 server

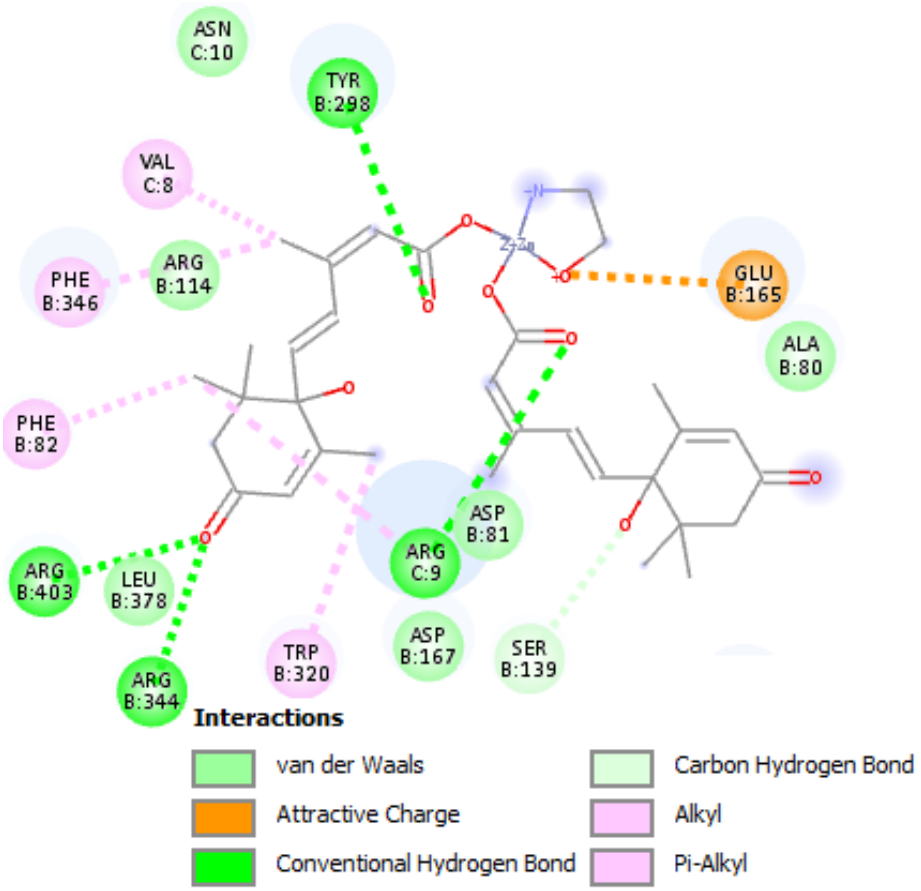


Fig. 4. Contact residues in the active site of the protein in 2P1O-Zn(ABA)$_2$(MEA)$_1$ complex docked by CB-Dock2 server

In addition, GLU165 is involved in the charge-charge interaction, enhancing the compound-protein interaction in the complex. A similar effect takes place in the $[Ni(ABA)_2(MEA)]$ coordination compound. There are no drastic changes in the interaction of type $[Me(ABA)_2(MEA)_2]$ compounds with proteins compared to type $[Me(ABA)_2(MEA)_2]$ compounds.

Conclusion

As a result of theoretical studies, it was established that the $[Zn(ABA)_2(MEA)]$ and $[Ni(ABA)_2(MEA)]$ complexes can have higher growth properties compared to the ABA compounds. This work may encourage chemists to synthesize coordination compounds $[Zn(ABA)_2(MEA)]$ or $[Ni(ABA)_2(MEA)]$ by reacting ABA with zinc or nickel salts.

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