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Communication

Bromelain: Unveiling Its Potential as a Natural Anti-Inflammatory Agent through Effective Binding to Apoptosis-Associated Speck-like Containing CARD (ASC)

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Abstract: This theoretical study presents a novel perspective on the potential anti-inflammatory properties of Bromelain, a natural agent extracted from pineapple stems. The investigation explores the binding capabilities of Bromelain to Apoptosis-associated speck-like containing CARD (ASC), a crucial adapter molecule known for its involvement in inflammatory processes and inflammasome formation. For the first time, these findings suggest that Bromelain exhibits a notable affinity for ASC, indicating its promising role as a natural anti-inflammatory agent. This study sheds light on the molecular interactions that may contribute to Bromelain's therapeutic potential in modulating inflammatory responses.

Keywords: apoptosis-associated speck-like containing; bromelain; HDOCK SERVER

1. Introduction

The Apoptosis-associated speck-like containing CARD (ASC), also known as PYCARD, is a crucial adapter molecule in inflammatory processes. Its primary role involves the formation of inflammasomes, multiprotein complexes that activate caspases, leading to inflammation and programmed cell death. ASC comprises PYD and CARD domains, facilitating interactions with similar domains in other proteins for inflammasome assembly[1–3]. While inflammasome activation is vital for the immune response against infections and cell damage, excessive activation can contribute to chronic inflammatory, autoimmune, or metabolic diseases. Consequently, understanding and regulating ASC and inflammasome activity are significant areas of research for potential therapeutic interventions in inflammation-related disorders[4,5]. The aim of this concise investigation is to examine the interplay between Apoptosis-associated speck-like containing CARD (ASC) and Bromelain through computational methods.Bromelain, known for its capacity to modulate inflammatory states, is composed of enzymes with proteolytic activity primarily extracted from pineapple stems[6–8].

The computational method employed to scrutinize potential binding and interactions between ASC and Bromelain at a molecular level was the HDOCK Server.

Broadly speaking, this is a protein-protein or protein-DNA/RNA docking approach based on a hybrid algorithm, incorporating template-based modeling and ab initio free docking[9,10].

Comprehending these interactions may offer insights into how Bromelain could impact ASC-mediated processes, such as inflammasome assembly and inflammation. Given Bromelain's recognized anti-inflammatory properties, investigating its influence on ASC through computational approaches may enhance our understanding of its therapeutic potential in modulating inflammatory responses.

2. Material and Methods

The HDOCK server was employed to predict the binding complexes between two molecules, specifically proteins represented by PDB Code 6U7D (Bromelain precursor used as the receptor) and

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PDB Code 2KN6 (Apoptosis-associated speck-like protein containing a CARD in CHAIN A used as the ligand). This prediction was carried out using a hybrid docking strategy.

3. Results and Discussion

The objective of this brief study is to explore the interaction between Apoptosis-associated speck-like containing CARD (ASC) and Bromelain using computational methods. Bromelain, recognized for its ability to regulate inflammatory states, is a group of enzymes with proteolytic activity primarily extracted from pineapple stems[6–8].

The computational method employed for the analysis of potential binding and interactions between ASC and Bromelain at a molecular level was the HDOCK Server [9,10]. The primary findings are presented in Figure 1, illustrating the outcomes of the interaction study. Table 1 provides the docking results by the HDOCK Server, demonstrating an excellent docking score and potential affinity between Bromelain and Apoptosis-associated speck-like containing CARD. Additionally, Tables 2–5 outlines the residues at the interface between the two targets.

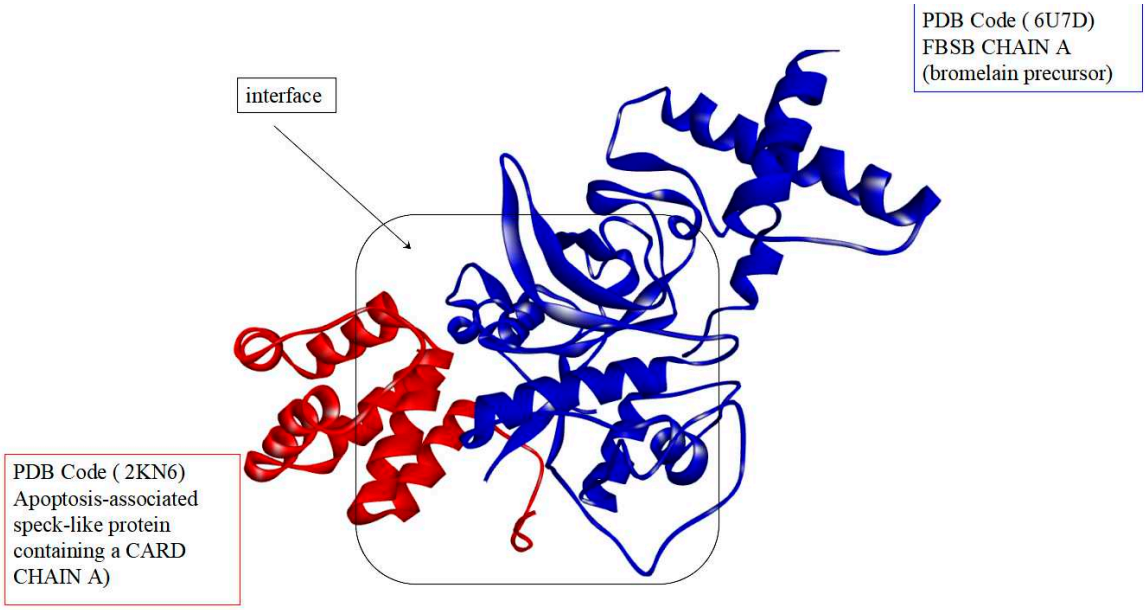

Figure 1. shows the binding region , highlighting the interaction between Bromelain (as the receptor, represented in blue) and Apoptosis-associated speck-like containing CARD (as the ligand, depicted in red).

Table 1. shows the docking results analysis, by HDOCK Server highlighting the interaction between Bromelain and Apoptosis-associated speck-like containing CARD .

Receptor (PDB ID: 6U7D-PDB Chain A ID:2KN6Chain A)	Docking Score (kcal/mol)	Confidence Score	Ligand rmsd(Å)
	-208.89	0.7646	62.17

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Table 2. shows Receptor interface residue(s) .

VAL	95A	2.149
ASP	96A	3.921
ALA	99A	2.707
ILE	104A	4.247
TRP	106A	3.988
ARG	107A	4.026
ASP	108A	2.023
TYR	109A	0.923
GLY	110A	2.807
ILE	136A	4.971
TYR	137A	1.729
LYS	138A	2.182
ILE	139A	1.108
LYS	140A	2.984
LYS	141A	4.059
GLY	142A	4.302
LEU	144A	4.118
ILE	174A	4.776
LYS	177A	3.584
ASN	201A	3.677
SER	202A	3.068
ALA	203A	3.243
TYR	204A	3.012
THR	206A	2.833
GLY	207A	3.447
TYR	208A	4.345
TYR	221A	0.946
SER	224A	3.491
LYS	225A	2.326
GLN	226A	3.104
TYR	310A	2.250
PRO	311A	3.689
THR	312A	2.204
LEU	313A	4.328
GLU	314A	2.966
SER	315A	2.853

Table 3. shows Ligand interface residue(s) .

MET	1A	2.149
GLY	2A	4.040
ARG	3A	0.946
ALA	4A	4.062
ARG	33A	2.182
GLU	34A	2.023
TYR	36A	2.728
TYR	60A	4.469
LEU	61A	0.923
GLU	62A	2.681
THR	63A	2.326
TYR	64A	3.020

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GLU	67A	1.108
LEU	68A	5.000
ASN	71A	3.297
ARG	74A	4.048
ALA	82A	4.754
GLY	83A	3.277
GLN	86A	2.853
ALA	87A	4.392
THR	89A	3.396
HIS	90A	2.204
GLN	91A	2.966
GLY	92A	2.899
SER	93A	3.447
GLY	94A	2.833
ALA	95A	3.422
ALA	96A	4.451
GLY	99A	3.584
ILE	100A	3.054
GLN	101A	3.012
ALA	102A	3.909
PRO	103A	1.729

Table 5. shows Receptor-ligand interface residue pair(s) .

95A	-	1A	2.149
95A	-	2A	4.040
96A	-	1A	4.397
96A	-	2A	4.167
96A	-	3A	3.921
99A	-	1A	2.707
99A	-	62A	3.792
104A	-	61A	4.247
106A	-	63A	4.365
106A	-	64A	4.076
106A	-	67A	3.988
107A	-	34A	4.026
108A	-	34A	2.023
108A	-	36A	2.728
109A	-	33A	4.188
109A	-	34A	4.144
109A	-	36A	3.403
109A	-	60A	4.469
109A	-	61A	0.923
109A	-	64A	3.020
110A	-	33A	2.807
110A	-	34A	4.173
136A	-	67A	4.971
137A	-	103A	1.729
138A	-	33A	2.182
138A	-	64A	4.683
139A	-	63A	4.681
139A	-	67A	1.108
139A	-	68A	5.000

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139A	-	71A	4.808
140A	-	67A	3.532
140A	-	71A	3.297
140A	-	74A	4.048
140A	-	86A	2.984
140A	-	89A	3.396
140A	-	90A	4.614
141A	-	71A	4.518
141A	-	74A	4.059
141A	-	86A	4.584
142A	-	33A	4.302
142A	-	71A	4.416
144A	-	33A	4.118
174A	-	100A	4.776
177A	-	99A	3.584
177A	-	100A	3.687
201A	-	103A	3.677
202A	-	103A	3.068
203A	-	103A	3.243
204A	-	100A	3.054
204A	-	101A	3.012
204A	-	102A	3.909
204A	-	103A	3.145
206A	-	92A	4.127
206A	-	93A	4.399
206A	-	94A	2.833
206A	-	95A	3.422
206A	-	96A	4.451
207A	-	93A	3.447
207A	-	94A	4.592
207A	-	95A	4.741
208A	-	93A	4.345
221A	-	3A	0.946
221A	-	62A	4.666
224A	-	63A	3.491
225A	-	3A	2.779
225A	-	4A	4.062
225A	-	62A	2.681
225A	-	63A	2.326
225A	-	67A	4.109
225A	-	89A	3.650
226A	-	90A	3.104
310A	-	90A	2.250
311A	-	90A	3.689
312A	-	90A	2.204
312A	-	91A	4.804
312A	-	92A	2.899
312A	-	93A	4.147
313A	-	86A	4.328
313A	-	90A	4.368
313A	-	92A	4.823
314A	-	87A	4.392

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314A	-	90A	4.473
314A	-	91A	2.966
314A	-	92A	4.093
314A	-	95A	4.088
315A	-	74A	4.883
315A	-	82A	4.754
315A	-	83A	3.277
315A	-	86A	2.853

4. Conclusions

This theoretical study presents a novel perspective on the potential anti-inflammatory properties of Bromelain, a natural agent extracted from pineapple stems. The investigation delves into Bromelain's binding capabilities with Apoptosis-associated speck-like containing CARD (ASC), a pivotal adapter molecule implicated in inflammatory processes and inflammasome formation. This study unveils molecular interactions that may underpin Bromelain's therapeutic potential in modulating inflammatory responses.

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