correlated with many cancer types including breast cancer especially in the metastasis stage [32]. Results of docking are elucidated in **Table 3**.

Table 3. PatchDock as well as FireDock results of the best anticancer peptides.

Peptides	PatchDock			FireDock				
	Score	**Area**	**ACE**	**Global Energy**	**Attractive VdW**	**Repulsive VdW**	**ACE**	**HB**
	EGFR							
Peptide 5	7600	992.4	-122.52	-19.35	-22.85	25.33	0.22	-2.13
Peptide 7	6794	831.8	-126.24	-56.01	-24.31	5.60	-12.86	-1.25
Peptide 10	7726	918.1	-43.34	-10.70	-22.41	9.27	11.81	-4.82
	ER-α							
Peptide 5	7834	999.2	-275.33	-63.55	-27.06	9.59	-17.47	-0.25
Peptide 7	7200	964.3	-420.73	-23.91	-29.78	72.17	-21.71	-1.8
Peptide 10	7022	945.7	-449.44	-63.35	-23.21	7.73	-20.42	-0.35
	MMP-3							
Peptide 5	6330	867.4	-337.62	-52.11	-25.57	10.42	-9.55	-1.93
Peptide 7	6220	695	-58.32	-38.91	-23.04	4.12	-4.92	-3.42
Peptide 10	6542	803.2	-181.46	-38.16	-19.16	8.64	-9.15	-0.34

ACE: Atomic Contact Energy; VdW: Van der Waal; HB: Hydrogen Bonds

As shown in **Table 3**, peptide 7 greatly blocks EGFR with a global energy of -56.01 kcal/mole while the remaining peptides are not good enough for EGFR inhibition. With respect to ER-α, peptide 5 as well as peptide 10 are superior inhibitors with a global energy -63.55 and -63.35 kcal/mole. Of the top 3 peptides, peptide 5 are good candidate for inhibition of MMP-3 (global energy -52.11 kcal/mole) whilst peptides 7 and 10 had a global energy of -38.91 and -38.16 kcal/mole. Collectively, peptide 7 is a good candidate for blockade of EGFR whereas peptide 5 can be used as inhibitor of both ER-α and, along with peptide 10, MMP-3. Peptide-protein interactions of best poses are shown in **Figure 2**. These data suggest that the studied peptides fragmented from *N.sativa* can be utilized as ACP against breast cancer receptors. Surprisingly, peptide 7 and peptide 5 are even better than the reference inhibitors of EGFR and ER-α (Erlotinib and TAM) in terms of global energy estimated by FireDock (-50.90 and -60.2 kcal/mole; data not shown).

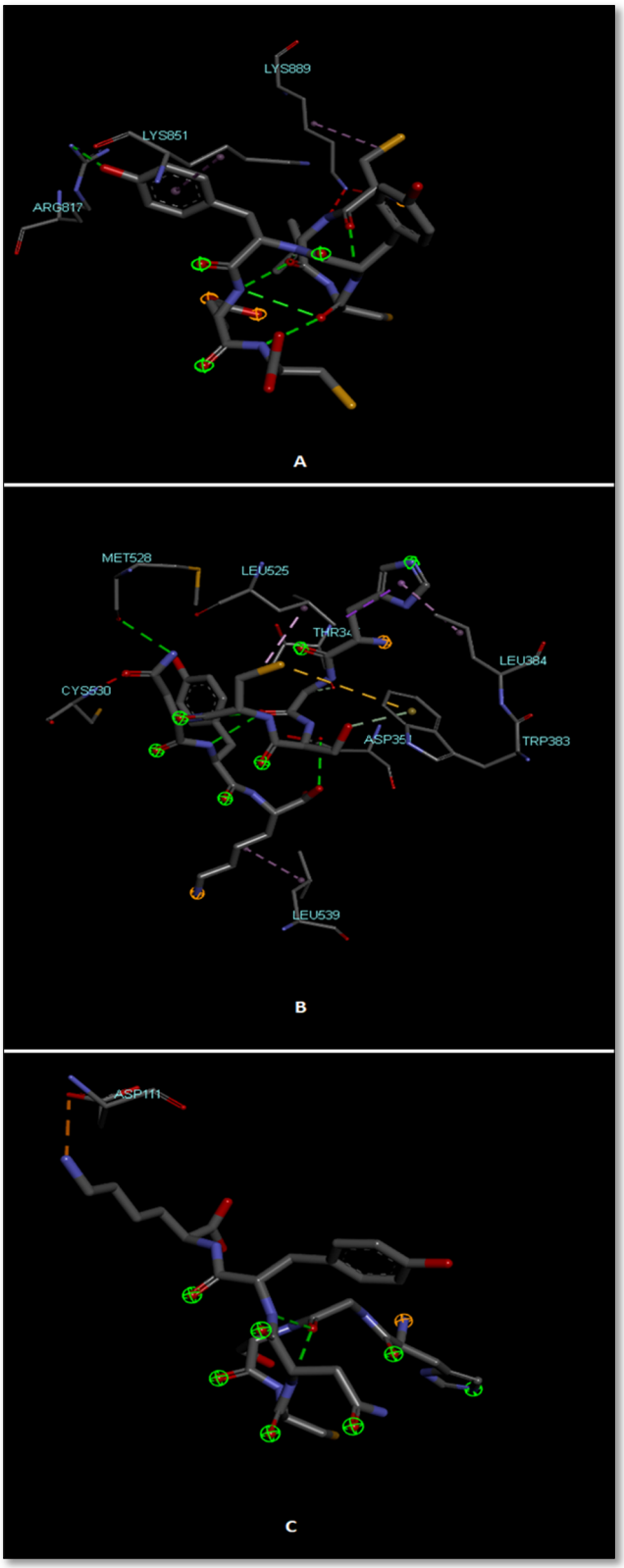

Figure 2. Peptide-protein docking 3D interaction visualized by discovery studio 2021. Docking results of peptide 7 against EGFR (A), peptide 5 against ER-α (B), and peptide 5 against MMP-3 (C).

EGFR interacted with peptide 7 through VdW interactions imposed by two lysine residues within the active site pocket and one arginine residue through H-bonds. Similarly, Asp 351 and Met 528 formed H-bonds with peptide 5 and the rest interacting residues interacted via VdW forces with ER-α. Regarding MMP-3, peptide 5 formed electrostatic attractions with Asp 111 **(Figure 2)**.

Accordingly, the present work demonstrates *in-silico* the anti-cancer activity of the peptides fragmented from some *N.sativa* proteins as predicted by ACPred and mACPred webservers and then validated by peptide-protein docking through PatchDock-FireDock platform. This candidates N.sativa as a superior source as therapeutic nutraceutical option against breast cancer theoretically.

CONCLUSION

In conclusion, 6 *N.sativa* proteins after proteolysis using trypsin enzyme gave rise to 23 peptides for which physico-chemical properties were calculated. 11 of which had ACP bioactivity as predicted by mACPred and ACPred platforms. Among them, peptides 5 (HGSCNYK), peptide 7 (CICYYEC), and peptide 10 (TCSGLCGCK) were the best in terms of the possibility score as ACP against 3 types of breast cancer receptors, EGFR, ER-α and MMP-3 as demonstrated by PatchDock and FireDock servers which necessitate *in vitro* assays confirmation. However, further analysis of the top peptides against wide array of other cancer types should be addressed. Also, the peptides with low anti-cancer activity should be assessed for different bioactivities.

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