References:

1. Plazas, M., Andújar, I., Vilanova, S., Hurtado, M., Gramazio, P., Herraiz, F. and Prohens, J. Breeding for Chlorogenic Acid Content in Eggplant: Interest and Prospects. *Notulae Botanicae Horti Agrobotanici Cluj-Napoca*, **2013,** *41*(1), p.26.
2. Kumar, N., Kumari, B., Singh, H., Ranganath, H., Shivakumara, B. and Kalleshwaraswamy, C. Pheromone trapping protocols for brinjal shoot and fruit borer, *Leucinodes orbonalis* Guenee (Lepidoptera: Pyralidae): evaluation of trap design, quantity and dispenser. *Journal of Horticultural Science*, **2006**, *1*(1), pp.39-43.
3. Ahmad, H., Rahman, M., Haque, M. and Ahmed, K. Studies on shoot and leaf characters of brinjal plants and their quantitative relationships with brinjal shoot and fruit borer. *Journal of Bangladesh Agricultural University*, **2009**, *7*, pp.29–32.
4. Bruce, T. and Pickett, J. Perception of plant volatile blends by herbivorous insects—finding the right mix. *Phytochemistry*, **2011**, *72*, pp.1605–1611.
5. Law, J. and Regnier, F. Pheromones. *Annual Review of Biochemistry*, **1971**, *40*(1), pp.533-548.
6. Cork, A., Alam, S., Rouf, F. and Talekar, N. Female sex pheromone of brinjal fruit and shoot borer, *Leucinodes orbonalis* (Lepidoptera: Pyralidae): trap optimization and application in IPM trials. *Bulletin of Entomological Research*, **2003**, *93*(2), pp.107-113.
7. Chidawanyika, F., Mudavanhu, P. and Nyamukondiwa, C. Biologically Based Methods for Pest Management in Agriculture under Changing Climates: Challenges and Future Directions. *Insects*, **2012**, *3*, pp.1171–1189.
8. Dethier, V., Brown, L. and Smith, C. The designation of chemicals in terms of the responses they elicit from insects. *Journal of Economical Entomology*, **1960**, *53*, pp.134 – 136.
9. Nordlund, D. and Lewis, W. Terminology of chemical releasing stimuli in intraspecific and interspecific interactions. *Journal of Chemical Ecology*, **1976**, *2*, pp. 211 – 220.

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Young Scientists' Circle

Unraveling the bioactivity of peptide-based nano systems in tumourgenesis

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Antimicrobial peptides (AMPs) are known as natural antibiotics produced by animals, plants, and bacteria. Even though AMPs have been identified as the most promising alternative to conventional molecules used against infections, some of them may have other activities such as defense mechanisms, or even regenerative. Moreover, the reported studies show the broad spectrum of cytotoxic activity against various types of cancer cells by these peptides. When considering the cell targets, some peptides active against microbial and cancer cells while not being active against healthy mammalian cells, such as magainins.[1] Some are active against all three types of cells including microbial, normal, and cancerous such as human neutrophil defensins HNP-1.[2] Although ACPs are expected to be selective toward tumor cells without impairing the normal cells, the development of a selective ACP has been regarded as a therapeutic strategy to explore.

From a structural point of view, the peptide with anti-cancer activities (ACPs) contain 5–50 amino acid chains and are generally composed of α-helices, β-sheets, or both.[3] Concerning the ACPs anticancer effects, it may generally occur by membranolytic mechanisms.[4] The anticancer activity is dependent on the peptide amphipathicity, hydrophobicity, as well as on the target membrane features such as protein receptors,[5] which in turn modulate the peptides' selectivity and toxicity.

However, the use of peptides as therapeutics has been limited by low bioavailability, poor stability to

proteolytic degradation, low permeability across barriers, and short biologic half-life in the circulatory system. Encapsulation of these peptides on nanocarriers may improve the potential of these therapeutic molecules to create a novel environment for therapeutics, disease diagnosis, fluorescent microscopy, imaging, and other life science devices.

Peptide nanotherapeutics have been reported useful tools in targeting and deliver the drug *in situ* to selectively target cancer cells, decreasing toxicity on healthy cells. Nanoparticles (NPs) offer the possibility to encapsulate poorly soluble anticancer drugs, enhance the stability of therapeutic molecules, and modify their blood circulation. The present study was focused to develop and characterize an *in vitro* sustained release formulation for peptide-based drugs using nanomaterials. The study focused to optimize a nanohybrid for a peptide.

In this study, a naturally derived 6-mer peptide was synthesized by the Solid Phase Peptide Synthesis (SPPS) method and characterized using nuclear magnetic resonance spectroscopy (NMR) and mass spectrometry (MS). The synthesized peptide was screened for *in vitro* cytotoxicity against Muscle rhabdomyosarcoma (RD) and Kidney normal (Vero) cell lines using 3, 4, 5-(dimethylthiazol-2-yl)-2-5-diphenyl tetrazolium bromide (MTT) cell viability assay. The native peptide effectively inhibited the survival of the rhabdomyosarcoma cell line in a dose-dependent manner with less cytotoxicity effect on a normal healthy cell line.

Furthermore, the undergoing molecular mechanism was studied using computational approaches. The *in silico* study revealed that the tumor inhibition by the peptide involves inhibition of an intracellular molecular pathway known as the serine/threonine kinase Akt signaling pathway, which is hyperactivated in rhabdomyosarcoma. The present study used docking and (un)binding simulation analyses to identify peptide interacting residues of the human target protein. The results proved that peptide is an allosteric inhibitor of the respective protein and exerts its inhibitory mechanism by binding to the allosteric site of the protein and engaging the functionally important residues in various interactions. The exact binding mode of the peptide-based on the computational approach is presented and various interacting residues within the allosteric site of this protein were identified and characterized. The docked peptide-protein conformation is expected to serve as a suitable model for understanding the amino-acid environment mediating molecular interactions and thus, providing details for the inhibitory mechanism of the peptide. In the future, this study will help to design novel peptidomimetics for human target protein isoforms and it will help experimental biologists in testing and designing better inhibitors.

In addition to the cytotoxicity and undergoing inhibitory mechanism of the peptide, we proved that it could increase the efficacy of the peptide against RD cells when it is encapsulated with drug carriers such as functionalized HNT (fHNT). The induced cytotoxicity effect permits the use of relatively low concentrations of peptides and drugs to achieve significant anticancer effects *in vitro*. This dose reduction minimizes drug side effects on normal cells and enables an effective apoptosis-mediated anticancer effect. Our present study has implications in that the peptide may become a promising anticancer therapeutic agent with high anticancer selectivity and a strong induced effect in combination therapy. Our studies mainly illustrate the mechanism of peptide-induced cell death and may be helpful in the design of chemotherapeutics against RMS cell lines.

In the future, the bioavailability of the peptide after release from fHNT composites can be confirmed by *in vitro* studies using kinetic assays. The research can be taken further to the next level with *in vivo* studies on different animal models. Further, the tubular ends and surface of drug-loaded fHNT can be modified with pH-sensitive polymers, followed by the preparation of oral tablets for gastrointestinal drug delivery.[6,7] Such aminosilane functionalized nanomaterials have been used in some previous studies, and they displayed no toxicity upon oral consumption.[7] These milestones by aminosilane modified nanomaterials indicate the promising usage of the peptide-loaded fHNT.

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References :

1. Fremeau, R. T.; Duncan, G. E.; Fornaretto, M. G.;

Dearry, A.; Gingrich, J. A.; Breese, G. R.; Caron, M. G. Localization of D1 Dopamine Receptor MRNA in Brain Supports a Role in Cognitive, Affective, and Neuroendocrine Aspects of Dopaminergic Neurotransmission. *Proc. Natl. Acad. Sci. U. S. A.* **1991**, *88* (9), 3772–3776. https://doi.org/10.1073/pnas.88.9.3772.

2. Varkey, J.; Nagaraj, R. Antibacterial Activity of Human Neutrophil Defensin HNP-1 Analogs without Cysteines. *Antimicrob. Agents Chemother.* **2005**, *49* (11), 4561–4566. https://doi.org/10.1128/AAC.49.11.4561-4566.2005.

3. Biswaro, L. S.; Sousa, M. G. d. C.; Rezende, T. M. B.; Dias, S. C.; Franco, O. L. Antimicrobial Peptides and Nanotechnology, Recent Advances and Challenges. Front. *Microbiol.* **2018**, *9* (MAY), 1–14. https://doi.org/10.3389/fmicb.2018.00855.

4. Brown, T. Deisign Thinking. *Harv. Bus. Rev.* **2008**, *86* (6), 84–92. https://doi.org/10.1002/med.

5. Gabernet, G.; Gautschi, D.; Müller, A. T.; Neuhaus, C. S.; Armbrecht, L.; Dittrich, P. S.; Hiss, J. A.; Schneider, G. In Silico Design and Optimization of Selective Membranolytic Anticancer Peptides. *Sci. Rep.* **2019**, *9* (1), 11282. https://doi.org/10.1038/s41598-019-47568-9.

6. Lvov, Y.; Wang, W.; Zhang, L.; Fakhrullin, R. Halloysite Clay Nanotubes for Loading and Sustained Release of Functional Compounds. *Adv. Mater.* **2016**, *28* (6), 1227–1250. https://doi.org/10.1002/adma.201502341.

7. Massaro, M.; Lazzara, G.; Milioto, S.; Noto, R.; Riela, S. Synthesis , Properties , Biological And. *J. Mater. Chem. B* **2017**, *5*, 2867–2882. https://doi.org/10.1039/c7tb00316a.

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Young Scientists' Circle

In Silico Study of potential drug leads for inhibition of angioensin converting enzyme using Sri Lankan Natural Products

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Almost fifty percent of the active ingredients present in modern medicine is derived from natural products. Natural products were widely used in the past for drug discovery before high-throughput screening and genomic sequencing were practiced. These natural product-based drugs are mostly derived from different organisms, such as plants, microbes and animals as well as a few synthetic or semi-synthetic compounds that are derived from natural products, including tigecycline, everolimus, micafungin and caspofungin.[1] These natural product-based drugs have been used for a range of medicinal indications and they have a wide diversity of chemical structures. Approximately half (49%) of the 877 small-molecule New Chemical Entities (NCEs) introduced between 1981 and 2002 were natural products, semi-synthetic natural product analogues or synthetic compounds based on pharmacophores of natural products.[2]

Studies show that natural products usually have a higher number of chiral centers than either synthetic drugs or compounds derived from combinatorial libraries, and they have increased steric complexity. While a slightly higher number of nitrogen-, sulphur- and halogen-containing groups appear to be present in drugs and combinatorial molecules, natural products on the other hand, carry a higher number of oxygen atoms[3]. Multivariate statistical study of molecular descriptors shows that the ratio of aromatic ring atoms to total heavy atoms (lower in natural products), the number of solved hydrogen bond donors and acceptors (higher in natural products) and higher molecular rigidity of hydrogen bond donors and acceptors (higher in natural