The Updated Review on Plant Peptides and Their Applications in Human Health

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Abstract
Biologically active plant peptides, consisting of secondary metabolites, are compounds (amino acids) utilized by plants in their defense arsenal. Enzymatic processes and metabolic pathways secrete these plant peptides. They are also known for their medicinal value and have been incorporated in therapeutics of major human diseases. Nevertheless, its limitations (low bioavailability, high cytotoxicity, poor absorption, low abundance, improper metabolism, etc.) have demanded a need to explore further and discover other new plant compounds that overcome these limitations. Keeping this in mind, therapeutic plant proteins can be excellent remedial substitutes for bodily affliction. A multitude of these peptides demonstrates anti-carcinogenic, anti-microbial, anti-HIV, and neuro-regulating properties. This article's main aim is to list out and report the status of various therapeutic plant peptides and their prospective status as peptide-based drugs for multiple diseases (infectious and non-infectious). The feasibility of these compounds in the imminent future has also been discussed.

Keywords
Therapeutic plant peptides · Peptide-based drugs · Anti-carcinogenic · Anti-HIV · Antifungal · Ribosomal-Inactivating Proteins (RIPs)

Introduction
Plants can be exploited as a bioreactor for many therapeutic proteins, the majority of which are secondary metabolites and their derivatives. Nephroblastoma lymphoma and acute lymphoblastic leukemia are treated with paclitaxel and vincristine which are derived from Taxus brevifolia Nutt and Catharanthus roseus, respectively (Seca and Pinto 2018). Furthermore, ingenol mebutate and curcumin extracted from Euphorbia peplus L and Curcuma longa L being were tested in clinical trials for pancreatic, colorectal (Pan et al. 2012), and non-melanoma skin cancers (Seca and Pinto 2018). Notwithstanding, these peptide-based drugs are accompanied by unquestionable impediments, including toxicity, low abundance, complex multi-step synthesis, developmental stage-specific production, improper metabolism, poor absorption, poor systemic bioavailability, development of multi-drug resistance, and associated adverse health issues (Seca and Pinto 2018). These preordained constraints have compelled the scientific community to explore plants for other medicinal peptides.

In contrast to metabolite-based drugs, protein-based drugs have high therapeutic efficiency due to: (i) High specificity ergo fewer chances of interference with biological processes, thereby alleviating the toxicity, (ii) Performance of complex functions, (iii) High tolerance (Leader et al. 2008) and (iv) Varying charging of proteins/peptides due to existence of numerous functional groups thereby targeting different tissues of our body with varying pH (Reddy and Yang 2011). Although a multitude of therapeutic plant peptides has been identified, only a small number of them have found their way into databases i.e., research on the characterization of plant peptides has been left halfway or indeterminate (Leader et al. 2008 and references therein). This is due to: (i) the absence of high-throughput techniques, (ii) expensive and arduous, (iii) problems associated with protein stability. Nevertheless, therapeutic plant peptides appear propitious in...
peptide-based drugs for many diseases and are brought to the scientific community. This review article encapsulates therapeutic plant proteins and their implementation focusing on infectious and non-infectious diseases in light of this situation.

Infectious diseases encompass diseases caused by organisms (bacteria, viruses, fungi, parasites, nematodes). In contrast, non-infectious diseases constitute metabolic disorders (diabetes, obesity, cancer, cardiovascular, genetic disorders, neuroregulatory, and much more). This review might guide to development of peptide drugs for the treatment of various diseases and disorders (Fig. 1).

**Infectious Diseases**

**Anti-microbial activity of plant peptides/proteins**

Microbes are one of the leading causes of various infectious diseases like common cough, cold, influenza, etc. Owing to their ubiquitous nature, infectious diseases can be transmitted easily from anywhere. To protect our bodies from such conditions, antibiotics have been used. However, the consumption of many antibiotics has given rise to the problem of anti-microbial resistance and has rendered present anti-microbial drugs fruitless (Kaur et al. 2012). Therefore, the scientific community has taken a keen interest in identifying prospective anti-microbial agents from native sources, particularly plants. Plants produce an extensive range of Anti-microbial Peptides/Proteins (AMP) since these peptides act as the first line of defense against pathogens, hence dubbed as Pathogen Response/Pathogenesis-Related (P.R.) Proteins. Plant AMPs are tissue-specific and are expressed constitutively, having both polar and non-polar groups and positive charges. They are cysteine-rich residues, and they generate multiple (2–6) disulfide bonds, thereby granting them stability and resistance against proteases and chemicals (Hernández-Ledesma et al. 2009; Hernández-Ledesma and Hsieh 2017). In addition to this, plant AMPs are small, have high target specificity, simple configuration (structure), various modes of administration, quick modifications can be performed, and negligible antigenicity (Yadav and Batra 2015). Considering the characteristics mentioned above and advantages, plant AMPs have been used to develop novel, highly efficient drugs to resolve multi-drug resistance infections. The main drawback is that only a few (not more than thousands) have been structurally and functionally characterized. In this article, we will consider three main classes of microbes: Bacteria, Fungi and Viruses. This review also deals with the Pathogenesis—Related (PR) proteins from plants and their therapeutic applications.

![Fig. 1 Schematic representation of plants peptides displaying various therapeutic properties](image-url)
**Anti-bacterial activity**

Plant ABPs (Anti-Bacterial Proteins) had emerged as potential alternative for a new class of antibiotics, tackling the obstacle of multi-drug resistance pathogens. Purothionin, the introductory ABP, was extracted from *Triticum aestivum* to inhibit a multitude of bacteria, including *Xanthomonas campestris*, *Corynebacterium michiganensis*, and *Pseudomonas solanacearum* (Naider and Anglister 2009). The majority of these plant ABPs are positively charged (Kaur et al. 2012). They are highly antagonistic against a multitude of bacteria, even in lower concentrations. In contrast, some of them are highly specific. Nevertheless, though promising, only a few have been identified and characterized structurally and functionally (Naider and Anglister 2009). The amino acid sequence, location and number of cysteine residues are the key classification criteria for ABPs. There are several families such as defensins, thionins, lipid transfer proteins (LTR), snakins, cyclotides, thaumatin, etc.

Talking about the mechanism of action of ABPs, the most established notion is that ABPs will cause the breakage of bacteria when they come in contact with the negatively charged membrane (Pan et al. 2012). The strong selectivity of ABPs towards bacterial cells is due to the intrinsic negative charge of the bacterial cell membrane which protects the host cell against infection. Once the ABPs associate with the cell membrane, the ABP concentration builds until it reaches its threshold value (Girish et al. 2006). Upon attaining the threshold value ABP oligomers were generated to enter the membrane perpendicularly forming micelle-like structures (Barrel-Stave Model). Owing to the electrostatic interactions, ABPs assemble on bacterial membrane, manifesting like a carpet generating tension in the lipid membrane and subsequent phospholipids rearrangement. This results in varied membrane fluidity and membrane disruption (Carpet Model); ABPs, upon interacting with the polar head groups of the phospholipids, manifest into a transmembrane pore that provokes bends in the membrane, causing the adjacent layers of the pore to merge. Pore formation causes ion and metabolite efflux, membrane depolarization, deranging the respiratory mechanism, preventing cell wall formation, disrupting the membrane, ultimately leading to cell death (Toroidal Pore Model) (Girish et al. 2006). One of the primary purposes for producing ABPs is to overcome the challenge of antibiotic resistance. ABP drugs are multifarious and have a high potential of forming a new class of antibiotics with lower odds of bacterial resistance. Many proteins have been extracted from plants with high antibacterial activity having low IC₅₀ value (Half Maximal Inhibitory Concentration) and Minimal Inhibitory Concentration (MIC). Shepherin I and II, two glycine-histidine-containing peptides isolated from *Capsella bursa-pastoris* inhibits several gram-negative bacteria. Circulin A and B, macrocyclic peptides (Cyclotides) extracted from *Chassalia parviflora* inhibits a multitude of gram-positive and gram-negative bacteria, with Circulin B inhibiting both (Park et al. 2004). In *Chromobacterium violaceum*, the amino acid lysine had anti-QS and anti-biofilm properties. It was documented that at a concentration of 0.684 mM, lysine decreased biofilm development by 16%, chitinolytic activity by 88.3%, and EPS production by 12.5% after 24 hours. It might also be used as a key component in the synthesis of peptides/proteins and tested for use in the treatment of bacterial infections, perhaps lowering the need for traditional antibiotics (Champalal et al. 2018).

The chitin-binding peptides isolated from *Tulipa gesneriana* Tu-AMP-1 and Tu-AMP-2, affect a wide variety of bacteria, including *Agrobacterium rhizogenes*, *Curtobacterium flaccumfaciens*, *Erwinia carotovora*, and *Agrobacterium radiobacter*, having an IC₅₀ value of 11–20 μg/ml (Walsh et al. 2013). The ABPs mentioned above are some of the examples that have been structurally and functionally defined. A variety of ABPs with superior specificity and other novel properties is yet to be explored. Additionally, research should be focused on identifying novel ABPs having low toxicity, rapid mode of action and reported antibacterial peptides as shown in Table 1.

**Anti-fungal activity of plant peptides/proteins**

There have been high incidences of patients with threatening fungal infections, particularly those with a compromised immune system like AIDS, organ transplants, cancer, etc. The prolonged use of medicines they take for their therapy makes them vulnerable to potent fungal infections that can ultimately lead to death. The main challenge is that not many drugs are available for many conditions and, worst case, the absence of drugs for the treatment. Furthermore, another obstacle of drug resistance originates from extended drug utilization, rendering the current drug unusable. Correspondingly, we have to hunt for novel drugs, especially from natural sources like plants. Antifungal Proteins/Peptides (AFP) are low molecular weight compounds that act as the first line of defense against fungal pathogens. These proteins include defensins, thionins, lipid-transfer proteins (LTR), chitinase-like proteins, lectins, etc. (Lee-Huang et al. 1991a). The majority of AFPs work by lysis of fungal cell wall or by targeting components like sphingolipids and chitin, thereupon inhibiting cell wall synthesis. One of the instances is that certain AFPs result in pore formation or membrane polarization upon binding of chitin on its conserve domain, causing an efflux of $K^+$ and influx of $Ca^{2+}$, ultimately cell lysis (Lee-Huang et al. 1991b). Some other examples of AFPs mechanism of action are of defensins. They follow receptor-mediated activation (Leader et al. 2008). Subsequent binding to this receptor causes ion...
| S. No | Plant and its part (Seeds) | Protein | Nature | M. Wt (kDa) | N-terminal sequence | Bacterial species (Tested) | *IC₅₀ | References |
|-------|---------------------------|---------|--------|-------------|---------------------|---------------------------|-------|------------|
| 1     | *Vigna sesquipedalis*     | Sesquin | Peptide | 7           | KTCENLADTY          | *M. phlei*                | 87 ± 5 µM | Wong and Ng (2005b) |
|       |                           |         |        |             |                     | *B. megaterium*            | 105 ± 5 µM | |
|       |                           |         |        |             |                     | *B. subtilis*              | 98 ± 2 µM | |
|       |                           |         |        |             |                     | *P. vulgaris*              | 75 ± 6 µM | |
| 2     | *Phaseolus lunatus L.*    | Lunatusin| Peptide | 7           | KTCENLADTFRGPCFATSNC | *M. phlei*                | 96 ± 9 µM | Wong and Ng (2005a) |
|       |                           |         |        |             |                     | *B. megaterium*            | 115 ± 6 µM | |
|       |                           |         |        |             |                     | *B. subtilis*              | 98 ± 5 µM | |
|       |                           |         |        |             |                     | *P. vulgaris*              | 81 ± 6 µM | |
| 3     | *Cycas revoluta*          | Cy-AM P1| Peptide | 4.58        | KGAPCAKKPCGPGHLHYKVD | *C. michiganensi*          | 7.3 µg/ml | Yokoyama et al. (2008) |
|       |                           |         |        |             |                     | *C. flaccumfaciens*        | 8.9 µg/ml | |
|       |                           |         |        |             |                     | *A. radiobacter*           | 8.3 µg/ml | |
|       |                           |         |        |             |                     | *A. rhizogenes*            | 8.5 µg/ml | |
|       |                           |         |        |             |                     | *E. carobora*              | 8.0 µg/ml | |
|       |                           | Cy-AMP2 | Peptide | 4.57        | KGAPCAKKPCGPGHLHYKVD | *C. michiganensi*          | 7.6 µg/ml | |
|       |                           |         |        |             |                     | *C. flaccumfaciens*        | 8.3 µg/ml | |
|       |                           |         |        |             |                     | *A. radiobacter*           | 7.8 µg/ml | |
|       |                           |         |        |             |                     | *A. rhizogenes*            | 8.2 µg/ml | |
|       |                           |         |        |             |                     | *E. carobora*              | 8.1 µg/ml | |
|       |                           | Cy-AMP3 | Peptide | 9.27        | AVTCNTVTSLSACPVPPFA  | *C. michiganensi*          | 235 µg/ml | |
|       |                           |         |        |             |                     | *C. flaccumfaciens*        | 195 µg/ml | |
|       |                           |         |        |             |                     | *A. radiobacter*           | 260 µg/ml | |
|       |                           |         |        |             |                     | *A. rhizogenes*            | 235 µg/ml | |
|       |                           |         |        |             |                     | *E. carobora*              | 230 µg/ml | |
| 4     | *Phytolacca americana*    | Pa-AMP-1| Protein | 3.94        | –                   | *B. megaterium*            | 8 µg/ml  | Liu et al. (2000)   |
|       | (Seeds)                   |         |        |             |                     | *S. aureus*                | 11 µg/ml | |
|       |                           |         |        |             |                     | *S. faecalis*              | > 300 µg/ml | |
| 5     | *Impatiens balsamina*     | B-AMP1  | Peptide | 2.46        | QWGRCCGWPGGRYVCVRWC  | *B. subtilis*              | 10 µg/ml | Tailor et al. (1997) |
|       | (Seeds)                   |         |        |             |                     | *M. luteus*                | 10 µg/ml | |
|       |                           |         |        |             |                     | *S. aureus*                | 30 µg/ml | |
|       |                           |         |        |             |                     | *S. faecalis*              | 6 µg/ml  | |
|       |                           | B-AMP4  | Peptide | 2.52        | QYGRCCNWPGGRYCRW     | *B. subtilis*              | 5 µg/ml  | |
|       |                           |         |        |             |                     | *M. luteus*                | 5 µg/ml  | |
|       |                           |         |        |             |                     | *S. aureus*                | 20 µg/ml | |
|       |                           |         |        |             |                     | *S. faecalis*              | 5 µg/ml  | |
|       |                           |         |        |             |                     | *X. campestris*            | 6 µg/ml  | |
|       |                           |         |        |             |                     | *X. oryzae*                | 15 µg/ml | |
## Table 1

| S. No | Plant and its part          | Protein   | Nature          | M. Wt (kDa) | N-terminal sequence | Bacterial species (Tested)          | *IC$_{50}$       | References          |
|-------|----------------------------|-----------|-----------------|-------------|---------------------|-------------------------------------|-----------------|---------------------|
| 6     | *Capsella bursapastoris* (Roots) | Shepherin I | Peptide        | 2.36        |                     | *E. coli*                          | <2.5 µg/ml | Park et al. (2000)  |
|       |                            |           |                 |             |                     | *P. putida*                         | <2.5 µg/ml |
|       |                            |           |                 |             |                     | *P. syringae*                       | <2.5 µg/ml |
|       |                            |           |                 |             |                     | *S. typhimurium*                    | <2.5 µg/ml |
|       |                            |           |                 |             |                     | *Serratia sp.*                      | 8 µg/ml    |
|       |                            |           |                 |             |                     | *B. megaterium*                     | 6 µg/ml    |
| 7     | *Mirabilis jalapa* (Seeds)   | Mj-AMP1   | Homodimeric peptide | 8           | –                   | *B. megaterium*                     | 6 µg/ml    | Cammue et al. (1992) |
|       |                            | Mj-AMP2   | Homodimeric peptide | 7           | –                   | *B. lutea*                          | 100 µg/ml  |
|       |                            |           |                 |             |                     | *B. megaterium*                     | 2 µg/ml    |
|       |                            |           |                 |             |                     | *S. lutea*                          | 50 µg/ml   |
| 8     | *Psidium guajava* (Seeds)    | Pg-AMP1   | Peptide         | 6.0         | –                   | *Klebsiella sp.*                    | ND          | Pelegrini et al. (2008) |
| 9     | *Withania somnifera* (Root tubers) | WSG   | Glycoprotein    | 28          | –                   | *B. subtilis*                       | ND          | Girish et al. (2006) |
|       |                            |           |                 |             |                     | *P. fluorescens*                     |            |
|       |                            |           |                 |             |                     | *C. michiganensis sub. sp. michiganensis* |            |
|       |                            |           |                 |             |                     | *X. oryzae pv. oryzae*              |            |
|       |                            |           |                 |             |                     | *X. axanopodis pv. malvaearum*      |            |
| 10    | *Ficus glomerata* (Leaves)   | NA        | Protein         | 35          | –                   | *S. enterica*                       | ND          | Thapliyal et al. (2016) |
|       |                            |           |                 |             |                     | *P. aeruginosa*                     |            |
|       |                            |           |                 |             |                     | *E. coli*                           |            |
|       |                            |           |                 |             |                     | *B. subtilis*                       |            |
| S. No | Plant and its part | Protein | Nature | M. Wt (kDa) | N-terminal sequence | Bacterial species (Tested) | *IC$_{50}$ References | References |
|-------|-------------------|---------|--------|------------|---------------------|---------------------------|-------------------------|---------|
| 11    | *Foeniculum vulgare* Mill. (Seeds) | Elute1  | Protein mixture | –          |                     | *S. aureus*               | 27.64 µg/ml             | al Akeel et al. (2017) |
|       |                   | Elute2  | Protein mixture | 34.4–48   |                     | *E. coli*                 | 67.56 µg/ml             |                     |
|       |                   |         |                     |           |                     | *P. aeruginosa*           | 28.01 µg/ml             |                     |
|       |                   |         |                     |           |                     | *P. vulgaris*             | 59.68 µg/ml             |                     |
|       |                   | Elute3  | Protein mixture | –          |                     | *S. aureus*               | 25.91 µg/ml             |                     |
|       |                   | Elute4  | Protein mixture | –          |                     | *E. coli*                 | 64.12 µg/ml             |                     |
|       |                   |         |                     |           |                     | *P. aeruginosa*           | 68.33 µg/ml             |                     |
|       |                   |         |                     |           |                     | *P. vulgaris*             | 57.83 µg/ml             |                     |
|       |                   |         |                     |           |                     | *S. aureus*               | 21.27 µg/ml             |                     |
| 12    | *Murraya koenigii* L. (Leaves) | APC     | Protein            | 35        |                     | *E. coli*                 | 60.52 µg/ml             |                     |
|       |                   |         |                     |           |                     | *P. aeruginosa*           | 25.02 µg/ml             |                     |
|       |                   |         |                     |           |                     | *P. vulgaris*             | 41.24 µg/ml             |                     |
|       |                   |         |                     |           |                     | *S. aureus*               | 20.8 µg/ml              |                     |
|       |                   |         |                     |           |                     | *B. subtilis*             | 41.06 µg/ml             |                     |
|       |                   |         |                     |           |                     | *E. coli*                 | 26.67 µg/ml             |                     |
|       |                   |         |                     |           |                     | *S. typhi*                | 35.67 µg/ml             |                     |
|       |                   |         |                     |           |                     | *V. cholerae*             | ND                     | Ningappa et al. (2010) |
| 13    | *Chassalia parviflora* (Whole Plant) | Circulin A | Macrocyclic peptides | 3.17      | -                   | *S. aureus*               | ND                     | Tam et al. (1999)     |
|       |                   | Circulin B | Macrocyclic peptides | 3.30      | -                   | *C. keyfyr*               | ND                     |                     |
|       |                   |         |                     |           |                     | *C. tropicalis*           | ND                     |                     |
|       |                   |         |                     |           |                     | *E. coli*                 | ND                     |                     |
|       |                   |         |                     |           |                     | *P. vulgaris*             | ND                     |                     |
|       |                   |         |                     |           |                     | *K. oxytoca*              | ND                     |                     |
|       |                   |         |                     |           |                     | *S. aureus*               | ND                     |                     |
| S. No | Plant and its part | Protein | Nature | M. Wt (kDa) | N-terminal sequence | Bacterial species (Tested) | *IC$_{50}$ | References |
|-------|-------------------|---------|--------|-------------|---------------------|---------------------------|-----------|------------|
| 14    | *Spinacia oleracea* (Leaves) | So-D1   | Peptide | 2.29        | –                   | *C. michiganensis*         | 1 µM      | Segura et al. (1998) |
|       |                   | So-D2   |         | 5.80        |                     | *R. solanacearum*          | 15 µM     |            |
|       |                   | So-D6   |         | 2.55        |                     | *C. michiganensis*         | 1 µM      |            |
|       |                   | So-D7   |         | 4.23        |                     | *R. solanacearum*          | 1 µM      |            |
|       |                   |         |         |             |                     |                           |           |            |
| 15    | *Oldenlandia affinis* (Whole Plant) | Kalata B2 | Macrocyclic peptides | 2.9 | – | *S. aureus* (DA7127) | ND | Printing et al. (2010) |
|       |                   | Kalata B1 |         | 2.89        | –                   | *E. coli* (DA4201)         |           |            |
|       |                   |         |         |             |                     | *S. enterica* (DA6192)     |           |            |
| 16    | *Vigna unguiculata* (Seeds)  | Cp-thionin II | Peptide | 5.2 | – | *S. aureus* (ATTC 25923) | ND | Franco et al. (2006) |
|       |                   |         |         |             |                     | *E. coli* (ATTC25922)      |           |            |
|       |                   |         |         |             |                     | *P. syringae*               |           |            |
| 17    | *Pharbitis nil* (Seeds) | Prn-AMP1 | Peptide | 4.3 | – | *B. subtilis* | 38 µg/ml | Koo et al. (1998) |
|       |                   | Prn-AMP2 | Peptide | 4.2 | – | *B. subtilis* | 20 µg/ml |            |
| 18    | *Vigna angularis* (Seeds) | VaD1    | Peptide | 5.0 | – | *S. epidermidis* | 36.6 µg/ml | Chen et al. (2005b) |
|       |                   |         |         |             |                     | *X. campestris pv. vesicatoria* | 40.8 µg/ml |            |
|       |                   |         |         |             |                     | *S. typhimurium*            | 143.4 µg/ml |            |
|       |                   |         |         |             |                     | *B. cereus*                 | > 500 µg/ml |            |
|       |                   |         |         |             |                     | *E. coli*                   | > 500 µg/ml |            |
|       |                   |         |         |             |                     | *E. carotovora pv. carotovora* | 1000 µg/ml |            |
|       |                   |         |         |             |                     | *P. vulgaris*               | > 1000 µg/ml |            |
|       |                   |         |         |             |                     | *S. enteritidis*            | > 1000 µg/ml |            |
|       |                   |         |         |             |                     | *P. syringae pv. syringae*  | > 1000 µg/ml |            |
| 19    | *Phaseolus vulgaris* (Seeds) | Vulgarinin | Seeds | 7 | – | *M. phlei* | 87 ± 5 µM | Wong and Ng (2005c) |
|       |                   |         |         |             |                     | *B. megaterium*             | 105 ± 5 µM |            |
|       |                   |         |         |             |                     | *B. subtilis*               | 98 ± 2 µM |            |
|       |                   |         |         |             |                     | *P. vulgaris*               | 75 ± 6 M µM |            |
| S. No | Plant and its part | Protein | Nature | M. Wt (kDa) | N-terminal sequence | Bacterial species (Tested) *IC<sub>50</sub> | References |
|-------|--------------------|---------|--------|-------------|---------------------|---------------------------------------------|------------|
| 20    | **Tulipa gesneriana** (Tulip Bulbs) | Tu-AMP-1 Peptide | 4.9 | – | E. carotovora | 11 µg/ml | Fujimura et al. (2004) |
|       | Tu-AMP 2 Heterodimeric Peptide | 5 | – | A. radiobacter | 17 µg/ml |
|       |                                   |        |       | A. rhizogenes | 20 µg/ml |
|       |                                   |        |       | C. michiganensis | 17 µg/ml |
|       |                                   |        |       | C. flaccumfaciens | 15 µg/ml |
|       |                                   |        |       | E. carotovora | 15 µg/ml |
| 21    | **Solanum tuberosum** (Tubers) | Snakin-1 Peptide | 6.9 | M | C. michiganensis | 4 µM | Berrocal-Lobo et al. (2002) |
|       | Snakin-2 Peptide | 7.0 | MAISKALFAS LLLSLLLLEQ | C. michiganensis | 1 µM |
|       |                                   |        |       | R. meliloti | 8 µM |
| 22    | **Triticum aestivum** L. (Endosperm) | α-Purothionin Polypeptide | 6 | MKSCCRSTLG RNCYNLCRAR | P. solanacearum | ND | de Caleya et al. (1972) |
|       | β-Purothionin Polypeptide | 6 | MGSKGLKGVM VCLLILGLVL | X. phaseoli | ND |
|       |                                   |        |       | P. solanacearum | ND |
| 23    | **Viola odorata** (Whole Plant) | Cycloviolacin O2 Macrocyclic peptides | 3.14 | GIPCGESCVPW IPCISSAIGC SCKSKVCYRN | S. enterica (DA6192) | ND | |
|       |                                   |        |       | E. coli (DA4201) | |
|       |                                   |        |       | S. aureus (DA7127) | |
|       | Vaby A Macrocyclic peptides | 2.86 | – | S. enterica (DA6192) | ND | Printing et al. (2010) |
|       |                                   |        |       | E. coli (DA4201) | |
|       |                                   |        |       | S. aureus (DA7127) | |
|       | Vaby D Macrocyclic peptides | 3.06 | – | S. enterica (DA6192) | ND | |
|       |                                   |        |       | E. coli (DA4201) | |
|       |                                   |        |       | S. aureus (DA7127) | |
| 25    | **Beta vulgaris** (Leaves) | AX 1 Peptides | 5.0 | AICKKPSKFV KGACGRDADC EKACDQENWP GGVCVPFLRC ECQRSC | C. betica | 0.4–0.8 µM | Kragh et al. (1995) |
|       | AX2 Peptides | 5.1 | ATCRKPSMYF SGCFAEDTNQKACNRREDWP NGKCLVG-FKC ECQRPC | |

*IC<sub>50</sub> values indicate the concentration at which 50% inhibition is observed.
| S. No | Plant and its part       | Protein | Nature | M. Wt (kDa) | N-terminal sequence                     | Bacterial species (Tested)                                                                 | *IC<sub>50</sub> | References |
|-------|--------------------------|---------|--------|-------------|-----------------------------------------|-------------------------------------------------------------------------------------------|-----------------|------------|
| 26    | *Mirabilis expansa* (Roots) | ME1     | Protein | 27          | METMRLLFLL LTIWTTVVGS                  | *P. syringae* B, A. tumefaciens C58, A. rhizogenes ATCC15834, B. subtilis G13R, F. carotovora ATCC15713, X. campestris pv vesicatoria, R. leguminosarum, S. marcescens | ND              | Vivanco et al. (1999) |
|       |                          | ME2     | Protein | 27.5        | –                                       | *P. syringae* A. tumefaciens A. rhizogenes (ATCC15834), B. subtilis G13R, F. carotovora, X. campestris pv vesicatoria, R. leguminosarum, S. marcescens |                 |            |
| 27    | *Benincasa hispida* (Seeds) | Hispidalin | Peptide | 5.7         | –                                       | *E. coli* P. aeruginosa S. enterica S. aureus                                                                 | ND              | Sharma et al. (2014) |
| 28    | *Zizyphus jujuba* (Fruit) | Snakin-Z | Peptide | 3.3         | –                                       | *K. pneumoniae* B. subtilis S. aureus                                                                                     | ND              | Daneshmand et al. (2013) |
| S. No | Plant and its part | Protein | Nature | M. Wt (kDa) | N-terminal sequence | Bacterial species (Tested) | *IC$_{50}$ | References |
|-------|--------------------|---------|--------|-------------|--------------------|--------------------------|----------|-----------|
| 29    | *Fagopyrum esculentum* Moe-nch. (Seeds) | Fa-AMP1 | Peptide | 3.8 | AQCGAQGGGA TCPGGLCCSQ WGWCGSTPKY CGAGCQSNCK | *E. carotovora* | 11 µg/ml | Fujimura et al. (2003) |
|       |                    | Fa-AMP2 | Peptide | 3.9 | AQCGAQGGGA TCPGGLCCSQ WGWCGSTPKY CGAGCQSNCR | *A. radiobacter* | 17 µg/ml |          |
|       |                    |         |         |     |                                                 | *A. rhizogenes* | 24 µg/ml |          |
|       |                    |         |         |     |                                                 | *C. michiganensis* | 14 µg/ml |          |
|       |                    |         |         |     |                                                 | *C. flaccumfaciens* | 15 µg/ml |          |
|       |                    |         |         |     |                                                 | *E. carotovora* | 15 µg/ml |          |
| 30    | *Allium sativum* (Bulbs) | Alliumin | Protein | 13 | DDFLCAGGCL | *P. fluorescens* | ND | Xia and Ng (2005) |
| 31    | *Vicia faba* (Flower) | Fabatin-1 | Peptide | 5.2 | LLGRCKVKS NFHFIPCLTD HCSTVCRGEG YKGGDCHGLR RRCMCLC | *E. coli* | ND | Zhang and Lewis (1997) |
|       |                    | Fabatin-2 | Peptide | 5.20 | LLGRCKVKS NFNGPCLTD HCSTVCRGEG YKGGDCHGLR RRCMCLC | *P. aeruginosa* | ND |          |
|       |                    |         |         |     |                                                 | *E. hirae* | ND |          |
| 32    | *Moringa Oleifera* (Seeds) | MoCP | Dimeric protein | 13 | | | | Shebek et al. (2015) |
| 33    | *Zea mays* (Kernel) | MBP-1 | Peptide | 4.1 | RSGRGECRRQ CLRRHEGQPW | *C. michiganense ssp. Nebraskaense* | ND | Duvick et al. (1992) |
| 34    | *Vigna radiate* (Seeds) | VrD1 | Peptide | 5.1 | MERKTSFLF LLLVVASDV | *E. coli* | ND | Lin et al. (2007) |

*IC$_{50}$: Concentration of protein required for 50% growth inhibition, NA Not available, ND Not determined, Cy-AMP Cycad antimicrobial peptide, Pa-AMP-1 Phytolacca americana antimicrobial peptide, Ih-AMP1 Impatiens balsamina antimicrobial peptides, Pg-AMP Psidium guajava-antimicrobial peptide, WSG Withania somnifera glycoprotein, APC antioxidant protein from curry leaves, VaD1 Vigna angularis defending, *M. E. Mirabilis expansa*, MoCP *Moringa oleifera* cationic protein, MBP-1 Maize Basic Peptide 1, VrD1 *Vigna radiate* defending-1, Mj-AMP *Mirabilis jalapa* antimicrobial peptide
permeability and pore formation. Other AFPs cause various modifications in host cell signaling processes, leading to ROS generation (Reactive Oxygen Species), eventually leading to apoptosis. AX1 and AX2, thionin-like peptides that are cationic, interact with anionic phospholipids causing fungal membrane permeabilization (Lee-Huang et al. 1991a; b). Thaumatin-like proteins, a class of AFPs, inhibit the fungal spore formation, leading to lysis. Pn-AMP-1 and Pn-AMP-2 (extracted from *Pharbitis nil*) hinder the hyphal growth, causing the tips to be shattered upon insertion of hyphae, ultimately leading to rupture of fungal membrane and cytoplasmic leakage (Leader et al. 2008). Like other plant peptides, AFPs are diverse, having inert anti-cancer and anti-HIV activity. Mungin, sesquin, lunatusin, and PHP (Peganum harmala protein) are examples (Lee-Huang et al. 1991a; b; Liu et al. 2000; Mazalovska and Kouokam 2018). The non-specific lipid transfer protein (nLTP) PHP, isolated from *Peganum harmala* have been shown to inhibit various fungal species with an IC50 value ranging 1.5–12.19 μM (Yokoyama et al. 2008). Hypotin (extracted from *Ara-chis hypogaea*) has been shown to inhibit the activity of species like *Pythium aphainerdermatum*, *Fusarium solani*, *Physalospora piricola*, *Alternaria alternata*, *Botrytis cinerea*, *Fusarium oxysporum*, and *Pythium aphainerderma-tum* (Stirpe et al. 1986). Vulgin inhibits the fungal activity of a wide variety of species, combined with potent anti-HIV activity by inhibiting HIV reverse transcriptase (Ye and Ng 2003). It was reported that a proteinaceous α-amylase inhibitor extracted from rhizome of *Cheilocostus specious* and purified employing anion exchange chromatography and column gel filtration had an activity on fungal α-amylase. The fungal activity was reduced by this 31.18 kDa protein from *C. specious* by 71% using ion-exchange chromatography and 96% using gel filtration (Balasubramanian et al. 2018). It was documented that *Ferula asafoetida* root was used to extract three major proteins with molecular weights of 14 kDa, 27 kDa, and 39 kDa. The 39-kDa protein significantly improved chymotrypsin activity, while the 14-kDa protein had antibacterial action towards *Pseudomonas aer-uginosa*. All three pure proteins were also reported to have significantly increased antioxidant activity (Chandran et al. 2017). Quorum-sensing inhibitors from Solanaceae family were also reported to possess anti-bacterial action against *Pseudomonas aeruginosa* (Singh et al. 2015).

Until now, hundreds of AFPs have been identified as having negligible toxicity. Tu-AMP-1 and Tu-AMP-2 are highly potent AFPs inhibiting *Fusarium oxysporum* and *Geotrichum candidum* (Wong and Ng 2005). Ginkobilobin (extracted from *Ginkgo biloba*) strongly affects the activity of *B. cinerea* (Wang and Ng 2000). Sesquin (extracted from *Vigna sesquipedalis*) is a highly active AFP with an IC50 value of 0.15 μM and 1.4 μM for *Mycosphaerella arachidicola* and *F. oxysporium*, respectively (Wani et al. 2020).

Despite all of these studies showing the therapeutic effects of AFPs, not many have reached clinical trials. Most of these peptides have been ignored due to a lack of proper classification and structural and functional diversity. Efforts in this direction are required so that the therapeutic potential of AFPs can be used to a full extent and the available AFPs are tabulated (Table 2).

**Anti-viral Activity of plant peptides and proteins**

**Anti-HIV Activity**

Acquired Immunodeficiency Syndrome (AIDS) is the fourth leading cause of death triggered by the Human immunodeficiency virus (HIV) (Irvin and Uckun 1992). Two variants of HIV are HIV-1 and HIV-2, each being etiologically and genetically different. Medically, these types vary with the disease’s pace of progression, with HIV-1 being faster than HIV-2 (Irvin and Uckun 1992). The mode of action of HIV-1 involves host and viral membrane interaction through binding of the envelope glycoproteins (g120 and gp41) to CD4, CCR5 and CXCR4 receptors of the host cell. Subsequently, the virus enters the cell along with the integration of the viral genome into the host genome (Wang 2012). Preventing protein maturation and viral RNA replication to DNA are some of the treatment options available to enhance the infected’s survivability. Nevertheless, no proper vaccine is available yet due to: (i) Advent of viral strains that are highly resistant to current anti-HIV drugs, (ii) Incapability to annihilate latent viruses, (iii) Toxicity, (iv) Lack of proper route of administration (Irvin and Uckun 1992). Hence, as mentioned earlier, the scientific community is probing novel drug molecules to curb the obstacle. Within this framework, therapeutic plant peptides are seen as prospective contestants. As an alternative, plant peptides can be used as an excellent medication due to their highly specific nature, increased bioactivity, non accumulated in our organs and less to negligible toxicity (Barbieri et al. 1982; Barbosa Pelegrini et al. 2011). Many antiviral plant proteins belong to the family of cyclotides endowed with a highly stable peptide framework. Cyclotides are cyclic structures that are 28–37 amino acid residues long. They consist of a cyclic cysteine knot motif (CCK) made up of highly conserved cysteine residues linked together by three disulfide bonds. Surface-exposed hydrophobic patches formed by the CCK motif and its cyclicity are some of the reasons for its anti-HIV activity (Gerlach and Mondal 2012). Some other plant proteins including RIPs (Ribosome Inactivating Proteins) such as TCS (Trichosanthin) and PAP (Pokeweed antiviral Protein-N-glycosidase that exhibits antiviral activity against several viruses) have strong anti-HIV potential with some present in clinical trials. TCS has
| S. No | Plant and its part | Protein | Nature | M.Wt. (kDa) | Peptide sequence | Fungal species (Tested) | *IC50 | References |
|-------|-------------------|---------|--------|-------------|-----------------|------------------------|-------|------------|
| 1     | *Momordica charantia* (Leaves) | MCha-Pr | Protein | 25.5 | VEYTTGNAGNTPGG | *A. brassicae* | 33 µM | *Zhang et al.* (2015) |
|       |                   |         |        |          |                 | *C. personata* | 42 µM |            |
|       |                   |         |        |          |                 | *F. oxysporum* | 37 µM |            |
|       |                   |         |        |          |                 | *Mucor* sp. | 40 µM |            |
|       |                   |         |        |          |                 | *R. solani* | 48 µM |            |
|       |                   |         |        |          |                 | *P. ananidermatum* | 18.9 µM | *Wang et al.* (2007) |
| 2     | *Arachis hypogaea* (Seeds) | Hypotin | Protein | 30.4 | CDVGSVISASLFE-ALQKHRN | *B. cinerea* | 7 µM | *Ye and Ng* (2003) |
|       |                   |         |        |          |                 | *A. alternate* | NA |            |
|       |                   |         |        |          |                 | *S. rolfsii* | NA |            |
|       |                   |         |        |          |                 | *F. oxysporum* | NA |            |
|       |                   |         |        |          |                 | *F. solani* | NA |            |
| 3     | *Phaseolus coccineus* cv. 'Major' (Seeds) | Coccinin | Peptide | 7 | KQTENLADTY | *M. arachidicola* | 75 ± 5 µM | *Ngai and Ng* (2004) |
|       |                   |         |        |          |                 | *F. oxysporum* | 81 ± 7 µM |            |
|       |                   |         |        |          |                 | *P. piricola* | 89 ± 4 µM |            |
|       |                   |         |        |          |                 | *B. cinerea* | 109 ± 5 µM |            |
|       |                   |         |        |          |                 | *C. comatus* | 122 ± 7 µM |            |
|       |                   |         |        |          |                 | *R. solani* | 134 ± 2 µM |            |
| 4     | *Phaseolus vulgaris* (Seeds) | Vulgin | Polypeptide | 5 | VDVGTVLTAT-FIEQQFKHRNDQAPEKG-GFYTYNAFISAAR | *B. cinerea* | 7 µM | *Ye and Ng* (2003) |
|       |                   | Fraction PTA2c | Peptide | 5 | KTCENLVDTYRGPCFT | *M. arachidicola* | NA |            |
|       |                   |         |        |          |                 | *B. cinerea* | 1 µM |            |
|       |                   |         |        |          |                 | *F. oxysporum* | NA |            |
| 5     | *Chrysanthemum coronarium* (Seeds) | Chrysancorin | Protein | 13.4 | RVDQKAQNLKKCCQKHFHRNDQAPEKG-GFYTYNAFISAAR | *B. cinerea* | 11 µM | *Wang et al.* (2001) |
|       |                   |         |        |          |                 | *M. arachidicola* | 17.4 µM |            |
|       |                   |         |        |          |                 | *P. piricola* | 14.6 µM |            |
|       |                   |         |        |          |                 | *F. oxysporum* | 1.9 µM |            |
|       |                   |         |        |          |                 | *B. cinerea* | 2.6 µM |            |
|       |                   |         |        |          |                 | *M. arachidicola* | 0.32 µM |            |
| 6     | *Phaseolus lunatus L.* (Seeds) | Lunatusin | Peptide | 7 | KTCENLADTFRGPC-FATSNC | *F. oxysporum* | 13.5 µM | *Wong and Ng* (2005a) |
|       |                   |         |        |          |                 | *H. maydis* | 27 µM |            |
|       |                   |         |        |          |                 | *M. arachidicola* | 10 µM |            |
|       |                   |         |        |          |                 | *B. cinerea* | 14.3 µM |            |
|       |                   |         |        |          |                 | *M. arachidicola* | NA |            |
| 7     | *Brassica juncea var. integrifolia* (Seeds) | Juncin | Protein | 18.9 | GVEVTRELRSERPSGKIVTI | *F. oxysporum* | 13.5 µM | *Ye and Ng* (2009) |
|       |                   |         |        |          |                 | *H. maydis* | 27 µM |            |
|       |                   |         |        |          |                 | *M. arachidicola* | 10 µM |            |
|       |                   |         |        |          |                 | *B. cinerea* | 14.3 µM |            |
| 8     | *Vigna angularis* (Seeds) | Angularin | Peptide | 8 | – | *B. cinerea* | 14.3 µM | *Ye and Ng* (2002b) |
|       |                   |         |        |          |                 | *M. arachidicola* | NA |            |
|       |                   |         |        |          |                 | *F. oxysporum* | 0.25 µM |            |
|       |                   |         |        |          |                 | *M. arachidicola* | 6.5 µM | *Wang and Ng* (2000) |
|       |                   |         |        |          |                 | *R. solani* | 3.6 µM |            |
|       |                   |         |        |          |                 | *C. comatus* | 8.7 µM |            |
| 9     | *Ginkgo biloba* (Seeds) | Ginkbilobin | Protein | 13 | – | *P. sasakii Ito* | ND | *Huang et al.* (2000) |
|       |                   |         |        |          |                 | *A. alternate* (Fries) Keissler | 3.4 µM |            |
|       |                   |         |        |          |                 | *F. oxysporum* | 1.8 µM | *Wang and Ng* (2003) |
|       |                   |         |        |          |                 | *M. arachidicola* | 1.4 µM |            |

| 10    | *Dendrocalamus latiflora* Munro (Shoot) | Dendrocin | Protein | 20 | – | *B. cinerea* | 1.8 µM | *Wang and Ng* (2003) |
| S. No | Plant and its part            | Protein     | Nature     | M.Wt. (kDa) | Peptide sequence | Fungal species (Tested) | *IC₅₀       | References                  |
|-------|------------------------------|-------------|------------|-------------|------------------|------------------------|------------|-----------------------------|
| 11    | *Vigna sesquipedalis* (Seeds) | Sesquin     | Peptide    | 7           |                  | *B. cinerea*          | 2.5 µM     | Wong and Ng (2005b)         |
|       |                              |             |            |             |                  | *F. oxysporum*        | 1.4 µM     |                             |
|       |                              |             |            |             |                  | *M. arachidicola*     | 0.15 µM    |                             |
| 12    | *Withania somnifera* (Root tubers) | WSG       | Glycoprotein | 28          |                  | *A. flavus*           | ND         | Girish et al. (2006)        |
|       |                              |             |            |             |                  | *A. niger*            |            |                             |
|       |                              |             |            |             |                  | *A.nidulans*          |            |                             |
|       |                              |             |            |             |                  | *A. flaviceps*        |            |                             |
|       |                              |             |            |             |                  | *A. alternate*        |            |                             |
|       |                              |             |            |             |                  | *A. carthami*         |            |                             |
|       |                              |             |            |             |                  | *F. oxysporum*        |            |                             |
|       |                              |             |            |             |                  | *F. verticilloides*   |            |                             |
| 13    | *Allium sativum* (Bulbs)     | Alliumin    | Protein    | 13          |                  | *M. arachidicola*     | 1.3 µM     | Xia and Ng (2005)           |
| 14    | *Pharbitis nil* (Seeds)      | Pn-AMP1     | Peptides   | 4.29        |                  | *B. cinerea*          | 16 µg/ml   | Koo et al. (1998)           |
|       |                              |             |            |             |                  | *C. langenarium*      | 10 µg/ml   |                             |
|       |                              |             |            |             |                  | *S. sclerotiorum*     | 11 µg/ml   |                             |
|       |                              |             |            |             |                  | *F. oxysporum*        | 10 µg/ml   |                             |
|       |                              |             |            |             |                  | *R. solani*           | 26 µg/ml   |                             |
|       |                              |             |            |             |                  | *P. capsici*          | 5 µg/ml    |                             |
|       |                              |             |            |             |                  | *P. parasitica*       | 3 µg/ml    |                             |
|       |                              |             |            |             |                  | *Pythium spp.*        | N.A        |                             |
|       |                              |             |            |             |                  | *S. cerevisiae*       | 14 µg/ml   |                             |
|       |                              |             |            |             |                  | *B. cinerea*          | 2 µg/ml    |                             |
|       |                              |             |            |             |                  | *C. langenarium*      | 4 µg/ml    |                             |
|       |                              |             |            |             |                  | *S. sclerotiorum*     | 3 µg/ml    |                             |
|       |                              |             |            |             |                  | *F. oxysporum*        | 2.5 µg/ml  |                             |
|       |                              |             |            |             |                  | *R. solani*           | 75 µg/ml   |                             |
|       |                              |             |            |             |                  | *P. capsici*          | 0.6 µg/ml  |                             |
|       |                              |             |            |             |                  | *P. parasitica*       | 2 µg/ml    |                             |
|       |                              |             |            |             |                  | *Pythium spp.*        | 2.5 µg/ml  |                             |
|       |                              |             |            |             |                  | *S. cerevisiae*       | 8 µg/ml    |                             |
| 15    | *Beta vulgaris* L. (Leaves)  | IWF4        | Dimeric protein | 4.5         |                  | *C. beticola*         | ≤ 2 µg/ml  | Nielsen et al. (1997)       |
|       |                              |             |            |             |                  |                       | (0.7 µM)   |                             |
| 16    | *Eucommia ulmoides* Oliv (Bark) | EAFP1     | Peptides   | 4.20        |                  | *A. lycopersici*      | 155 µg/ml  | Huang et al. (2002)         |
|       |                              |             |            |             |                  | *F. moniliforme*      | 56 µg/ml   |                             |
|       |                              |             |            |             |                  | *F. oxysporum*        | 46 µg/ml   |                             |
|       |                              |             |            |             |                  | *C. gossypii*         | 35 µg/ml   |                             |
|       |                              |             |            |             |                  | *A. lycopersici*      | 109 µg/ml  |                             |
|       |                              |             |            |             |                  | *F. moniliforme*      | 18 µg/ml   |                             |
|       |                              |             |            |             |                  | *F. oxysporum*        | 94 µg/ml   |                             |
|       |                              |             |            |             |                  | *C. gossypii*         | 56 µg/ml   |                             |
|       |                              |             |            |             |                  |                       |            |                             |
| S. No | Plant and its part       | Protein Nature | M.Wt. (kDa) | Peptide sequence | Fungal species (Tested) | *IC50 | References                  |
|-------|--------------------------|----------------|-------------|------------------|-------------------------|-------|-----------------------------|
| 17    | Capsella bursa-pastoris (Roots) | Shepherin I Peptide | 2.36        |                  | C. albicans < 2.5 µg/ml | 8 µg/ml | Park et al. (2000)          |
|       |                          | Shepherin II Peptide | 3.26        |                  | C. neoformans < 2.5 µg/ml | 7 µg/ml |                              |
|       |                          |                |             |                  | S. cerevisiae 7 µg/ml    |       |                              |
|       |                          |                |             |                  | A. alternate 7 µg/ml     |       |                              |
|       |                          |                |             |                  | A. flavus 65 µg/ml       |       |                              |
|       |                          |                |             |                  | A. fumigatus > 100 µg/ml | > 100 µg/ml |                          |
|       |                          |                |             |                  | F. culmorum 72 µg/ml     |       |                              |
|       |                          |                |             |                  | C. albicans 5 µg/ml      |       |                              |
|       |                          |                |             |                  | C. neoformans < 2.5 µg/ml |       |                              |
|       |                          |                |             |                  | S. cerevisiae 3 µg/ml    |       |                              |
|       |                          |                |             |                  | A. alternate > 100 µg/ml | > 100 µg/ml |                          |
|       |                          |                |             |                  | A. flavus 60 µg/ml       |       |                              |
|       |                          |                |             |                  | A. fumigatus > 100 µg/ml | > 100 µg/ml |                          |
|       |                          |                |             |                  | F. culmorum 68 µg/ml     |       |                              |
| 18    | Hevea brasiliensis (Latex) | Hevein Protein | 4.7         |                  | B. cinerea 500 µg/ml     |       | van Parijs et al. (1991)   |
|       |                          |                |             |                  | F. culmorum 600 µg/ml    |       |                              |
|       |                          |                |             |                  | F. oxysporum 1.25 mg/ml |       |                              |
|       |                          |                |             |                  | P. blakesleeanus 300 µg/ml |       |                              |
|       |                          |                |             |                  | P. triticirepentis 350 µg/ml |       |                              |
|       |                          |                |             |                  | P. oryzae 500 µg/ml      |       |                              |
|       |                          |                |             |                  | S. nodorum 500 µg/ml     |       |                              |
|       |                          |                |             |                  | T. hamatum 90 µg/ml      |       |                              |
|       |                          |                |             |                  | A. alternate 51 µg/ml    |       | Kiba et al. (2005)          |
|       |                          |                |             |                  | B. cinerea 61 µg/ml      |       |                              |
|       |                          |                |             |                  | F. solani 99 µg/ml       |       |                              |
|       |                          |                |             |                  | R. solani 30 ± 4 µM      |       | Lam and Ng (2010)           |
| 19    | Gentiana triflora (Leaves) | GtAFP1 Protein | 20          |                  | F. oxysporum 2 µg/ml     |       | Fujimura et al. (2004)      |
|       |                          |                |             |                  | G. candidum 2 µg/ml      |       |                              |
|       |                          |                |             |                  | A. alternate 1.56–12.5 µg/ml |       |                              |
|       |                          |                |             |                  | C. tropicalis, C. parapsilosis 1.56 µM |       |                              |
|       |                          |                |             |                  | M. arachidica 5.5 µM     |       | Ye and Ng (2002b)           |
| 20    | Acacia confusa (Seeds)    | Acaconin Protein | 32          |                  | M. arachidica 1.3 µM     |       | Kumar et al. (2014)         |
|       |                          |                |             |                  | B. cinerea 1.56–12.5 µg/ml |       |                              |
| 21    | Tulipa gesneriana (Tulip Bulbs) | Tu-AMP1 Peptide | 4.9         |                  | F. oxysporum 2 µg/ml     |       | Wong and Ng (2003a)         |
|       |                          | Tu-AMP2 Dimeric peptide | 2.259     |                  | G. candidum 2 µg/ml      |       | Ye and Ng (2001)            |
| 22    | Cicer arietinum (Seeds)   | CLAP Protein | 18          |                  | M. arachidica 5.5 µM     |       |                              |
|       |                          | C-25 Lectin protein | 25          |                  | B. cinerea 1.3 µM        |       |                              |
| 23    | Gymnocladus chinensis Baill (Beans) | Gymnin Peptide | 6.5         |                  | F. oxysporum 2 µM        |       |                              |
| 24    | Adzuckia angularia (Seeds) | Fraction AB2 Peptide | 5          |                  | M. arachidica 3.5 µM     |       |                              |
| S. No | Plant and its part     | Protein          | Nature   | M.Wt. (kDa) | Peptide sequence       | Fungal species (Tested)     | *IC₅₀       | References                   |
|-------|------------------------|------------------|----------|-------------|------------------------|-----------------------------|------------|------------------------------|
| 25    | Macadamia integrifolia (Seeds) | MiAMP1          | Peptide  | 5.9         |                        | C. michiganensis            | 50 µg/ml   | Marcus et al. (1999)         |
| 26    | Vigna angularis (Seeds)  | VaD1             | Peptide  | 5.0         |                        | F. oxysporum sp. pisi       | 30 µg/ml   | Chen et al. (2005b)          |
| 27    | Phaseolus vulgaris (Seeds) | Vulgarinin       | Peptide  | 7           | KTCENLADTYKGP CFTSGGD  | B. cinerea                  | 2.9 µM     | Wong and Ng (2005c)          |
|       |                        |                  |          |             |                        | F. oxysporum                | 1.7 µM     |                              |
|       |                        |                  |          |             |                        | M. arachidica               | 2.2 µM     |                              |
|       |                        |                  |          |             |                        | C. albicans                 | 0.21 µM cc|                              |
| 28    | Spinacia oleracea (Leaves) | So- D2          | Peptide  | 5.80        |                        | F. culmorum                 | 0.2 µM     | Segura et al. (1998)         |
|       |                        | So-D6           | Peptide  | 2.55        |                        | F. solani                   | 0.2 µM     |                              |
|       |                        | So-D7           | Peptide  | 4.23        |                        | F. culmorum                 | 11 µM      |                              |
| 29    | Actinidia chinensis (Fruit) | Kiwi TLP        | Protein  | 21          |                        | M. arachidica               | 0.43 µM    | Wang and Ng (2002)           |
|       |                        |                  |          |             |                        | C. albicans                 | 8 µM       |                              |
| 30    | Benincasa hispida (Seeds) | Hispidalin       | Peptide  | 5.7         |                        | A. flavus                   | ND         | Sharma et al. (2014)         |
|       |                        |                  |          |             |                        | F. solani                   | ND         |                              |
|       |                        |                  |          |             |                        | G. candidida                | ND         |                              |
|       |                        |                  |          |             |                        | P. chrysogenum              | ND         |                              |
|       |                        |                  |          |             |                        | C. gloeosporioides          | ND         |                              |
| 31    | Peganum harmala (Seeds)  | PHP              | Homodimeric protein | 18         |                        | A. alternate                | 1.5 µM     | Ma et al. (2013)             |
|       |                        |                  |          |             |                        | P. degitatum                | 7.5 µM     |                              |
|       |                        |                  |          |             |                        | R. stolonifer               | 8.44 µM    |                              |
| 32    | Cycas revoluta (Seeds)   | Cy-AMP1          | Peptide  | 4.58        |                        | F. oxysporum                | 6.0 µg/ml   | Yokoyama et al. (2008)       |
|       |                        | Cy-AMP2          | Peptide  | 4.56        |                        | G. candidum                 | 7.4 µg/ml   |                              |
|       |                        |                  |          |             |                        | F. oxysporum                | 7.1 µg/ml   |                              |
| 33    | Allium tuberosum (Shoot) | Cy-AMP3          | Peptide  | 9.27        |                        | G. candidum                 | 7.0 µg/ml   | Lam et al. (2000)            |
|       |                        | Fraction MS3     | Protein  | 36          |                        | F. oxysporum                | 0.2 µM      |                              |
| 34    | Dolichos lablab (Seeds)  | Dolichin         | Protein  | 28          |                        | R. solani                   | ND         | Ye et al. (2000)             |
been shown to lower HIV-1 p24 antigen levels in AIDS patients (Leader et al. 2008). MAP30 (Momordica anti-
human immunodeficiency virus protein) is a highly potent anti-HIV agent and a type-I RIP, with an IC$_{50}$ of only 0.33

\begin{table}[h]
\centering
\begin{tabular}{|c|c|c|c|c|c|c|}
\hline
S. No & Plant and its part & Protein & Nature & M.Wt. (kDa) & Peptide sequence & Fungal species (Tested) & *IC$_{50}$ & References \\
\hline
35 & Panax ginseng (Roots) & Panaxagin & Homodimeric protein & 53 & – & \textit{F. oxysporum} & ND & Ng and Wang (2001) \\
36 & Phaseolus mungo (Seeds) & Mungin & Protein & 18 & – & \textit{R. solani} & ND & Ye and Ng (2000) \\
37 & Zea mays (Kernels) & MBP-1 & Peptide & 4.13 & – & \textit{F. graminearum} & ND & Duvick et al. (1992) \\
38 & Raphanus sativus (Seeds) & RsAFP1 & Tetrameric poly-peptide & 20 & – & \textit{A. brassicola} & ND & Terras et al. (1992) \\
 & & RsAFP2 & Trimeric poly-peptide & 15 & – & \textit{A. brassicola} & ND & \\
39 & Zingiber officinalis (Rhizome) & G-24 & Protein & 24 & – & \textit{F. oxysporium} & 4.6 µM & Terras et al. (1992) \\
40 & Trichosanthes dioica (Seeds) & TDSC & Glyco-protein & 39 ± 1 EING GGA & & \textit{A. niger} & ND & Kabir et al. (2016) \\
\hline
*IC$_{50}$ Concentration of protein required for 50% growth inhibition, ND Not determined, NA Not available, as these proteins have been claimed to exhibit the activity, but no activity parameters have been mentioned, Kiwi TLP Kiwi fruit thaumatin-like protein, \textit{MCha-Pr} \textit{Momordica charantia} pathogenesis-related protein, \textit{Fraction PTA2c} Pinto bean antifungal peptide, \textit{WSG \textit{Withania somnifera} glycoprotein}, \textit{IWF4} Intercellular washing fluid, \textit{EAFP} \textit{Eucommia antifungal peptide}, \textit{GtAFP} \textit{Gentiana triflora antifungal protein}, \textit{MBP-1} \textit{Maize basic peptide}, \textit{CLAP} \textit{Chickpea cyclophilin-like antifungal protein}, \textit{VaD1} \textit{Vigna angularis} variegate 1, \textit{TDSC} \textit{Trichosanthes dioica} seed chitinase
\end{tabular}
\end{table}
PAP has been conjugated with TXU and attacks the CD7 antigen of HIV-infected cells, thereby inhibiting the infection (Lee-Huang et al. 1990).

Being prone to microbial infections, the combined activity of both anti-HIV and anti-microbial peptides could create new opportunities for HIV therapy. Aforementioned proteins have properly recorded structures, but not much research has been done to understand their mode of action. The most widely accepted hypothesis is attacking the viral envelope (Bokesch et al. 2004). The cyclotides work by viral membrane disruption leading to the formation of the pore (Gerlach and Mondal 2012). These cyclotides (Kalata 1) get bound to the phospholipid-rich viral coat with the help of its hydrophobic patches, resulting in an oligomeric form that penetrates the viral coat. This leads to the formation of discrete pores, thereby causing the coat to collapse (Wang 2012). As viral coat has glycoproteins in it, plant peptides like ricin and con A, possessing carbohydrate-binding sites in them, have been considered as potential candidates for inhibiting HIV at initial stages (Mazalovska and Kouokam 2018). RIPs like PAP, MAP30, TCS stop HIV-1 replication through depurination of long terminal repeats (LTRs) present in the DNA (Kaur et al. 2012). Another RIP saporin impedes the activity of HIV1 integrase for processing the 3' end of the viral DNA disintegrating genome and its mRNA (Yadav and Batra 2015). If we can decipher the role of such proteins at different phases of the viral infection, anti-HIV activity can be exploited. Steps are to be taken to extract and characterize much more powerful anti-HIV agents that are less toxic. The available anti-HIV peptides are reported in Table 3.

**Anti-SARS-CoV-2 activity**

SARS-CoV-2, also called COVID-19 (Coronavirus Disease 2019), has more than 130 million reported cases worldwide and has taken the lives of more than 2.8 million people since its onset in late 2019 (Zhou et al. 2020) and successive pandemic declarations by the WHO on 11 March 2020 (WHO 2021). Since the virus outbreak, a monumental effort has been made by researchers and drug companies worldwide to discover a vaccine. Multiple candidates were chosen from varied sources, most of them being in clinical trials. But so far, no definite cure has been developed. Only a few vaccines have been engineered as a contingency plan against the virus. Plant peptides have also been tested for vaccine production to broaden the range of candidates. Lectin extracted from red marine alga *Grifithsia* sp. (GRFT) have been shown to inhibit the cytopathic effect of SARS-CoV, enhancing the mortality of cells (O’Keefe et al. 2010). In the case of MERS-CoV (Middle East respiratory syndrome-CoV: Strain of SARS-CoV in the Middle East), GRFT acts by preventing its entry into the host cell through spike protein inhibition. Thus, GRFT serves as an effective inhibitor of MERS-CoV infection (Millet et al. 2016). In-silico methods using plant proteins have also been utilized to identify the potential lead compounds for COVID-19 vaccine design. Avenin from oats, α/β-gliadin from wheat, and ribulose bisphosphate carboxylase small chain from multiple sources have been utilized to generate effective binders to SARS-CoV-2 spike receptor-binding protein (RBD). When combined with certain oligopeptides (VQVVN, PISCR), these plant peptides / proteins might be employed as lead compounds in developing potent entry inhibitors (Luo et al. 2020). A wide variety of therapeutic plant peptides exist, out of which only a few have been explored (Mammari et al. 2021). Future research should focus on other plant-derived peptides, their mode of action, and their side effects in order to engineer a proper peptide vaccine for COVID-19.

**Non-infectious Diseases**

The diseases which are mainly caused due to environmental or genetic factors and not by pathogens are termed non-infectious diseases. Examples of non-infectious diseases include diabetes mellitus, most cancers, and cardiovascular diseases. These could be cured using therapeutic peptides obtained from various plant sources. Peptides are essential molecules that can attach to multiple cell surface receptors. The plant peptides used as drugs are increasing day by day. This review is majorly discuss the plant peptides with anti-diabetic, anti-cancer, and anti-hypertensive properties. When treated with proteolytic enzymes of plant proteins form protein hydrolysates and yield peptides. These therapeutic peptides could be used to treat various non-infectious diseases. Nineteen percent of the medicinal plant peptides are used to cure metabolic disorders, twelve percent are used to cure cancer, and almost three percent to cure cardiac related problems (Patil et al. 2020). The peptides obtained from various plant sources such as common bean, rice, pinto bean, hemp seeds, and mulberry have anti-diabetic properties. Peptides obtained from soybean, wheat, barley, and walnut have anti-cancer properties. Anti-hypertensive activity is observed in peptides purified from rice and walnut. This review focuses on the various peptides, their origins, sequences, and how they prevent non-infectious diseases (Table 4).

**Anti-diabetic activity of plant peptides/proteins**

Diabetes mellitus is widespread, and it is one of the most prevalent non-infectious diseases and its treatment is challenging. A study conducted in India, reports 80 million diabetic cases, and projected to be 140 million cases by 2037 (Deepthi et al. 2018). The increasing number of cases shows diabetic prevalence in India and the need
| S. No | Plant and its part       | Protein  | Nature | M. Wt. (kDa) | Peptide Sequence                                      | Mode of action                              | *IC₅₀  | References                     |
|-------|--------------------------|----------|--------|--------------|-------------------------------------------------------|----------------------------------------------|--------|-------------------------------|
| 1     | *Phaseolus lunatus* (Seeds) | Lunatusin | Peptide | 7            | KTCENLADTFRGPCKFATSNCP1                                    | HIV-1 reverse transcriptase inhibition         | 120 µM | Wong and Ng (2005a)           |
| 2     | *Phaseolus vulgaris* (Seeds) | Vulgin    | Polypeptide | 5          | VDVGTVTATFIEQFFKHRRNDAQPEGKGFYTNAFISAAR                      | HIV-1 reverse transcriptase inhibition         | 58 µM  | Ye and Ng (2003)              |
| 3     | *Lens culinaris* (Seeds) LTI | Fraction PTA2c Peptide | Peptide | 16   | GDKKKQAYTDYSTRSQQPP                                       | HIV-1 reverse transcriptase inhibition         | 258 µM | Ye and Ng (2001)              |
| 4     | *Vigna sesquipedalis* (Ground Beans) | Sesquin Peptide | Peptide | 7      | KTCENLADTY                                               | HIV-1 reverse transcriptase inhibition         | ND     | Ye and Ng (2005b)             |
| 5     | *Acacia confusa* (Seeds) N.A | Acaconin Protein | Protein | 32    | –                                                     | HIV-1 reverse transcriptase inhibition         | 73 µM  | Lam and Ng (2010)             |
| 6     | *Gelonium multiflorum* (Seeds) GAP 31 | GAP 31 Protein | Protein | 31    | –                                                     | HIV-1 reverse transcriptase inhibition         | 0.32 nM| Lee-Huang et al. (1991b)      |
| 7     | *Dianthus caryophyllus* (Leaves) DAPs 30 | DAPs 30 Protein | Protein | 30    | ATAYLNLAPSASQSYSXF                                       | HIV-1 reverse transcriptase inhibition Inhibition of syncytium formation | 0.28 nM|
|       |                           | DAPs 32 Protein | Protein | 32    | AVKTLNLVSPSANSRYATF                                      | HIV-1 reverse transcriptase inhibition Inhibition of syncytium formation | 0.88 nM|
| 8     | *Momordica charantia* (Seeds) MAP 30 | MAP 30 Protein | Protein | 30    | DVNFDLSTATAKTYTATLF                                        | HIV-1 reverse transcriptase inhibition Inhibition of viral core protein p24 expression | 0.33 nM|
|       |                           |           |        |      | Inhibition on syncytium formation                          |                                              | 0.22 nM| Lee-Huang et al. (1990)      |
| S. No | Plant and its part | Protein | Nature | M. Wt. (kDa) | Peptide Sequence | Mode of action | *IC$_{50}$ | References |
|-------|-------------------|---------|--------|-------------|-----------------|---------------|----------|------------|
| 9     | *Trichosanthes kirilowii* (Root tubers) | TAP 29  | Protein | 29          | –               | Inhibition of syncytium formation | 0.34 nM | Lee-Huang, et al. (1991a) |
|       |                   |         |        |             |                 | Inhibition of viral core protein p24 expression | 0.37 nM |
|       |                   |         |        |             |                 | Inhibition of viral-associated reverse transcriptase activity | 0.46 nM |
| 10    | *Dorstenia contrajerva* (Leaves) | Contrajervin  | Peptide | 5           | ERDDHRCGPDPYGNPSCSGDRCCSIYWNCGGGS-SCSegerQYQCWY | HIV-1 inhibition by binding to gp120 and gp41 | > 4.9 µM | Bokesch et al. (2004) |
| 11    | *Treculia obovoidea* (Bark) | Treculavirin  | Dimeric peptide | 10      | PGCEERPDHCQGPYNPCGGAGGRCSIHGWCGSSAYDSCSTSCQYQCSC | HIV-1 inhibition by binding to gp120 and gp41 | > 2.5 µM | Bokesch et al. (2004) |
| 12    | *Dolichos lablab* (Seeds) | Dolichin  | Protein | 28          | GAVGSVINA-SLFQQLKHRRNQDP-PEGKG | HIV-1 reverse transcriptase inhibition | < 180 µM | Ye et al. (2000) |
| 13    | *Oldenlandia affinis* | Kalata B 1 (Whole Plant) | Macrocyclic Peptides | 2.89 | GLPVCEGETCVGGTC-GTNG | HIV inhibition by cell envelope disruption | 3.5 µM | Daly et al. (2004) |
|       |                   | Kalata B 8 (Aerial Parts) | Macrocyclic Peptides | 3.28 | GSNLECGTCELLGCYTTG | HIV inhibition by cell envelope disruption | 11 µM | Daly et al. (2006) |
| 14    | *Chassalia parvifolia* | Circulin A (Crude Extract) | Macrocyclic Peptides | 3.17 | GIPCGESCVW IPCISAALGCSCKNKV-CYR N | HIV replication inhibition | 0.05 µM | Gustafson et al. (1994) |
|       | Circulin B (Crude Extract) | Macrocyclic Peptides | 3.3 | GIPCGESCVFIPCISTAALGCSCKNKV-CYR N | HIV replication inhibition | 0.05 µM | Gustafson et al. (1994) |
|       | Circulin C (Stems) | Macrocyclic Peptides | 3.1 | NA | NA | NA | Gustafson et al. (2000) |
|       | Circulin D (Stems) | Macrocyclic Peptides | 3.39 | NA | NA | NA | Gustafson et al. (2000) |
|       | Circulin E (Stems) | Macrocyclic Peptides | 3.39 | NA | NA | NA | Gustafson et al. (2000) |
|       | Circulin F (Stems) | Macrocyclic Peptides | 3.05 | NA | NA | NA | Gustafson et al. (2000) |
| 15    | *Peganum harmala* (Seeds) | PHP  | Homodimeric protein | 18 | – | HIV-1-RT inhibition | 1.26 µM | Ma et al. (2013) |
| 16    | *Palicourea condensata* (Bark) | Palicourein  | Polypeptide | 3.9 | RNGDPTFCGETCRVIPVCTYSAALGCTCD-DRSDGLCK | HIV-1 replication inhibition | 1.5 µM | Bokesch et al. (2001) |
| 17    | *Trichosanthes kirilowii* (Root tubers) | TCS or (GLQ 223) | Protein | 26 | – | HIV-1 replication inhibition | 0.46 nM | Shu et al. (2009) |
| S. No | Plant and its part | Protein | Nature | M. Wt. (kDa) | Peptide Sequence | Mode of action | *IC<sub>50</sub> | References |
|-------|-------------------|---------|--------|-------------|-----------------|---------------|-------------|------------|
| 18    | *Leonia cymosa* (Bark) | Cycloviol A | Macrocyclic peptides | 3.2 | SCVFIPCISAIGC-SCKNKVCY | NA | 0.56 μM | Hallock et al. (2000) |
|       |                   | Cycloviol B |               | 2.8 | SCYVLPCFTVGCCTTSSQ | | | |
|       |                   | Cycloviol C |               | 3.1 | SCVFIPCLTTVAGC-SCKNK | | | |
|       |                   | Cycloviol D |               | 3.1 | SCVFIPCISAIGC-SCKNKCY | | | |
| 19    | *Viola odorata* (Whole Plant) | Cycloviolacin O2 | Macrocyclic peptides | 3.1 | HIV inhibition by cell membrane disruption | NA | 6.4 μM | Ireland et al. (2008) |
|       |                   | Cycloviolacin O13 (Aerial Parts) | | 3.12 | | | 4.8 μM | |
|       |                   | Cycloviolacin O14 (Aerial Parts) | | 3.17 | | | | |
|       |                   | Cycloviolacin O24 (Aerial Parts) | | 3.04 | | | 6.17 μM | |
| 20    | *Viola yedoensis* (Whole Plant) | Cycloviol Y1 | Macrocyclic peptides | 3 | | NA | 4.47 μM | Wang et al. (2008) |
|       |                   | Cycloviol Y4 | | | | | 1.72 μM | |
|       |                   | Cycloviol Y5 | | | | | 1.76 μM | |
| 21    | *Viola tricolor* (Whole Plant) | Varv E | Macrocyclic peptides | 2.99 | | NA | 3.98 μM | Wang et al. (2008) |
| 22    | *Viola hederacea* (Leaves) | Vhl-1 | Macrocyclic peptides | 3.33 | | NA | 0.87 μM | Chen et al. (2005a) |
| 23    | *Vicia faba* cv. Giza 843 (Seeds) | VFTI-G1 | Protein | 15 | HIV-1-RT inhibition | 0.76 μM | | Dia and Krishnan (2016) |
| 24    | *Gymnocladus chinensis* Baill (Beans) | Gymnin | Peptide | 6.5 | HIV-1-RT inhibition | 200 μM | | Wong and Ng (2003b) |
| 25    | *Adzukia angularia* (Seeds) | Fraction AB2 | Peptide | 5 | HIV-1-RT inhibition | 280 μM | | Ye and Ng (2001) |
| 26    | *Bauhinia variegata* (Seeds) | Fraction BG2 | Homodimeric lectin | 64 | HIV-1-RT inhibition | 1.02 μM | | Chan and Ng (2015) |
| 27    | *Momontica balsamina* (Seeds) | Balsamin | Protein | 28 | HIV-1 replication inhibition | 10.2 nM | | Kaur et al. (2012) |
| 28    | *Phaseolus vulgaris* (Seeds) | Vulgarinin | Peptide | 7 | HIV-1-RT inhibition | 130 μM | | Wong and Ng (2005c) |
Table 3 (continued)

| S. No | Plant and its part | Protein Nature | M. Wt. (kDa) | Peptide Sequence | Mode of action | References |
|-------|-------------------|----------------|-------------|------------------|---------------|------------|
| 29    | Phytolacca americana (Leaves) | PAP Protein | 29 - 30 | - | Inhibited p24 production in HIV | Irvin and Uckun (1992) |
|       |                   | PAP-I         | 14 ± 2.1 nM | Asp, Val, Asp-Phe, Leu, Ser, Gly, Ala, Asp | HIV-1-RT inhibition | Rajamohan et al. (1999) |
|       |                   | PAP-II        | 17 ± 2.0 nM | Ser, Gly, Ala, Asp | HIV-1-RT inhibition | Jantakryjak et al. (2000) |
|       |                   | PAP-III       | 18 ± 2.0 nM | Ser, Gly, Ala, Asp | HIV-1-RT inhibition | Ye and Ng (2009) |
| 30    | Momordica charantia (Seeds) | MRK29 Protein | 28.6 | Asp, Val, Asp, Phe, Leu, Ser, Gly, Ala, Asp | HIV-1-RT inhibition | Jiratchariyakul et al. (2001) |
| 31    | Brassica juncea var. integrifolia (Seeds) | Juncin Protein | 18.9 | - | HIV-1-RT inhibition | Ye and Ng (2009) |
| 32    | Panax ginseng (Roots) | Panaxagin Homodimeric protein | 53 | - | HIV-1-RT inhibition | Ng and Wang (2001) |
| 33    | Allium tuberosum (Shoot) | Fraction MS3 Protein | 36 | EQHGSQAGGALH-PXHLSKYGGYGGTTPDYYGDGGQQ | HIV-1-RT inhibition | Lam et al. (2000) |

*IC$_{50}$ Concentration causing 50% inhibition, ND Not determined, NA Not available, as these proteins have been claimed to exhibit activity, but no activity parameters have been mentioned.

**LTI** Lentil trypsin-chymotrypsin inhibitor, **TAP** 29 Trichosanthes anti-HIV protein, **MAP** 30 Momordica anti-HIV protein, **Vhl-1** Viola hederacea leaf cyclotide-1, **MR-29** Thai anti-HIV protein

Several peptides in plants are reported to possess anti-diabetic property by controlling/inhibiting the enzymes and transporters associated with glucose metabolism (α-glucosidase inhibitors, α-amylase inhibitors, DPP-IV inhibitors, GLUT and SLUT) (Patil et al. 2020).

### α-Glucosidase Peptide Inhibitors

The outcome of Ren et al. (2016) study reported that *Cannabis sativa L.* (hemp seeds) peptide (Leucine-Arginine and Proline-Leucine-Methionine-Leucine-Proline) has α-glucosidase inhibitory activity. The hydrophobic nature of the amino acids proline and leucine has shown to have α-glucosidase inhibitory activity, which can be incorporated in therapeutic peptide for further development of effective anti-diabetics. Similarity, 14 amino acids (Tryptophan-glycine-valine-glutamate-asparagine-alanine-threonine-tyrosine-phenylalanine-tryptophan-glutamine-threonine-valine) long peptide from *Morus alba L.* (Mulberry) and a peptide (Threonine-threonine-glycine-glycine-lysine-glycine-lysine) from *Phaseolus vulgaris L.* (black bean) were shown to have α-glucosidase inhibitory activity (Jha et al. 2018; Mojica and Mejia 2016).

### α-Amylase Peptide Inhibitors

The peptide CSP-1 (cumin seed peptide) obtained from *Cuminum cyminum L.*, has shown 25 % of α-amylase inhibition property (Patil et al. 2020), whereas the peptide from *Phaseolus vulgaris cv. Pinto* (pinto beans) showed 62.10 % of inhibition. Seven peptides from pinto beans are reported to have α-amylase inhibition property and each of which are in 6–16 amino acids in length. One among the seven peptides which had higher inhibition activity is composed of proline-proline-histidine-methionine-leucine-proline (Ngoh and Gan 2016).

### Dipeptidyl Peptidase-IV (DPP-IV) Peptide Inhibitors

DPP-IV facilitates the degradation of Glucagon-like peptide-1 (GLP-1), hence DPP-IV inhibitors are the prime molecules in controlling diabetics. The proteases Umamizyme G and Bioprase SP containing Leucine-Proline and Isoleucine-Proline amino acids from *Oryza sativa* were having inhibitory activity against DPP-IV. Among which, Isoleucine-Proline was the most potent DPP-IV enzyme inhibitor with the IC$_{50}$ value of 2.5 mg/ml (Hatanaka et al. 2015).
GLUT and SLUT Plant-Based Peptide Inhibitors

GLUT and SLUT are to be inhibited during hyperglycemic condition where the blood glucose levels are highly elevated. Patil et al. 2020 reported that the peptides in black beans (*Phaseolus vulgaris L.*) have the ability to block the glucose transporters (GLUT-2 and SLUT-1) in order to control the elevated blood glucose level.

Anti-hypertensive activity of plant peptides/proteins

Hypertension, an elevated pressure in the blood vessels and it is one of the major causes of cardiovascular diseases. Renin-Angiotensinogen System (RAS) is mainly involved in the management of blood pressure. The inhibitors of these enzymes (renin and Angiotensin-I-Converting Enzyme (ACE) of RAS) inhibits the elevated vasodilators to control the blood pressure level. Daskaya-Dikmen et al. 2017 reported several plant-based peptides showing inhibitory activity against ACE towards the development of novel anti-hypertensive therapeutics.

Peptide Inhibitors of ACE

The peptide P-2a2 (Tryptophan-proline-glutamate-arginine-proline-proline-glutamine-isoleucine-proline) from walnut has the molecular weight of 1034 Da and it has shown higher level of inhibition profile with an IC\textsubscript{50} value of 23.67 μg/ml against ACE, which prevents the breakdown of vasodilator, bradykinin (Liu et al. 2013). The peptide (Leucine–Arginine–Alanine) obtained from *Oryza sativa* and chebulin (Aspartate–Glutamate–Asparagine–Serine–Phenylalanine) from *Terminalia chebula Retz* has shown anti-hypertension activity by inhibiting ACE. The walnut and the fruit of *Terminalia chebula Retz* have been used as a food supplement in the control the hypertension (Shobako and Ohinata 2020; Sornwatana et al. 2015).

Table 4 List of plant peptides/proteins used for non-infectious diseases

| S. No | Plant and its part | M. Wt | Sequence | Inhibitor target | Property | References |
|-------|-------------------|-------|----------|------------------|----------|------------|
| 1     | *Cannabis sativa L.* (Seeds) | 287.2 Da | LR PLMLP | Alpha-glucosidase inhibition | Anti-diabetic | Ren et al. (2016) |
| 2     | *Morus alba L.* (Leaves) | 0.3–5 KDa | WGVENAATY-FWQTV | Alpha-glucosidase inhibition | Anti-diabetic | Jha et al. (2018) |
| 3     | *Phaseolus vulgaris L.* (Fruit) | – | – | Alpha-glucosidase inhibition | Anti-diabetic | Mojica and de Mejía (2016) |
| 4     | *Phaseolus vulgaris L.* (Fruit) | > 3 kDa | – | Alpha-amylase inhibition | Anti-diabetic | Ngoh and Gan (2016) |
| 5     | *Oryza sativa L.* (Seeds) | – | – | DPP-IV enzyme inhibitor | Anti-diabetic | Hatanaka et al. (2015) |
| 6     | *Phaseolus vulgaris L.* (Fruit) | – | – | GLUT2 and SLUT1 inhibitor | Anti-diabetic | Patil et al. (2020) |
| 7     | Walnut (Fruit) | 1033.42 Da | WPERPPEIP | ACE inhibitor | Anti-hypertensive | Liu et al. (2013) |
| 8     | *Oryza sativa* (Husk) | – | – | ACE inhibitor | Anti-hypertensive | Shobako and Ohinata (2020) |
| 9     | *Terminalia chebula Retz* (Fruit) | 1033 Da | DENSKF | ACE inhibitor | Anti-hypertensive | Sornwatana et al. (2015) |
| 10    | *Oryza sativa* (Husk) | – | – | – | Anti-proliferative | Kannan et al. (2010) |
| 11    | *Glycine max* *Triticum aestivum* *Hordeum vulgare* *Amaranthus- hypochondriacs* (Fruit) | – | – | – | Anti-mitotic, anti-cancer | Hernandez-Ledesma et al. (2009) |
| 12    | *Juglans regia L.* (Fruit) | 621.2795 Da | CTLEW | – | Causes apoptosis and autophagy | Ma et al. (2015) |
antioxidant property than native soybean peptide. Similarly, Zhang et al. 2018 study shows the antioxidant peptides, valine-leucine-tyrosine-isoleucine-tryptophan (MW 673.1 Da) and serine-valine-proline-tyrosine-glutamate (MW 566.9 Da) were having potential antioxidant activity. Six peptides obtained from Pinto beans by Ngoh and Gan (2016) shown highest antioxidant activity.

Ribosome Inactivating Proteins and peptides from plants

Ribosome-Inactivating Proteins (RIPs) are a category of proteins whose principal function is to impair ribosomes in an irreversible manner modifying rapidly through enzymatic pathways (Stirpe 2004). Considering their discovery in the last few decades, RIPs investigation and inculcation in therapeutics have garnered tremendous scientific attention. RIPs are present in bacteria and plants, yet many plant RIPs have been well-characterized and have been traced to their functions compared to bacterial RIPs (Walsh et al. 2013). By hydrolyzing a specific N-C glycosidic bond of the eukaryotic 28S rRNA (belonging to the large 60S ribosomal subunit), the integral N-glycosidase activity of RIPs liberates the adenine residue from the 3’ end of its conserved GAGA tetraloop (sarcin/ricin loop), thereby impeding protein synthesis and irreversibly inactivating the ribosome (Walsh et al. 2013). RIPs have also been shown to exhibit RNase, DNase, polynucleotide adenosine glycosidase, superoxide dismutase activity (Park et al. 2006). RIPs have been classified into three subclasses, two of them being most prominently exploited for research purposes (Girish et al. 2006). The highly ubiquitous RIP-I is the most widely used RIP with a 26–35 kDa molecular weight. RIP-I launches itself into the cell by attaching to the LDL (Low-Density Lipoprotein) receptors (Walsh et al. 2013). The example of Saporin (Type I RIP extracted from Saponaria officinalis) can be used to understand the mechanism of protein synthesis inhibition by RIP-I. Internalization of saporin takes place through endocytosis by binding to the member of the LDL receptor family, α2-macroglobulin/LPR1 (low-density lipoprotein receptor-related protein1) existent in the host cell membrane (Vago et al. 2005). Saporin sets foot on cytoplasm through golgi independent pathway, thereby steering clear of low pH conditions of intracellular compartments. Once inside the cytoplasm, saporin inhibits protein synthesis by excising the adenine residue from the 3’ end of the particular site of the ribosome (Walsh et al. 2013). Another example of RIP-I, TCS (Trichosanthes kirilowii), associated with negatively charged phospholipid containing monolayer through electrostatic, hydrophobic interactions under acidic conditions (low pH), altering the charge of some residues, which is accompanied by salt-bridge breakage and charge to charge repulsion. This is followed by partial denaturation of TCS into a molten globular state, thus entering the host cell (Puri et al. 2012).

The process of protein synthesis inhibition is similar to that of any Type-I RIP. The RIP-II, is group of proteins is highly toxic. It is a heterodimeric carbohydrate-binding protein composed of 2 chains, A and B, held together by a disulfide bond. It has a molecular weight of 56–69 kDa, with each chain having a molecular weight of about 30 kDa (Girish et al. 2006). The A-chain exhibits vital N-glycosidase activity. The B-chain enables RIP-II to attach to the particular carbohydrate-containing cell receptors, as it has a strong affinity for carbohydrate moieties. This, in turn, leads to the migration of chain A across the cell membrane (Stirpe 2004). The entry process into cells for RIP-II is highly different from RIP-I because the latter lacks B-chain, which plays a vital role in its internalization process. Ricin (extracted from Ricinus communis) as almost all the Type-II RIPs are analogous to ricin, which has a well-identified for their mode of action (Puri et al. 2012). Binding to a particular receptor on the host cell membrane through the B-chain, ricin enters the cell either by clathrin-dependent or clathrin-independent endocytosis resulting in the origin of ricin containing endosomal vacuole (Puri et al. 2012). Eventually, ricin enters the trans-golgi network in COP-I vesicles. It is delivered to the early endosomes, either recycled by returning it to the cell surface or undergoes proteolytic degradation by the lysosome, finally reaching the E.R. lumen (Fujimura et al. 2004; Gustafson et al. 2000). The disulfide bond joining the two chains is degraded within the E.R. lumen, letting the remaining ricin transported by Endoplasmic Reticulum Associated Degradation (ERAD-Pathway for degradation of misfolded proteins) to the cytoplasm (Fujimura et al. 2004; Gustafson et al. 2000). Almost most of the toxin is degraded by 26s proteasome, leaving behind only a small portion that influences protein synthesis (Puri et al. 2012). Additionally, another class of RIP is not universal-Type-III RIPs. They show similar enzymatic activity to RIP-I as they have an identical N-terminal domain bound to the carboxyl domain with an unestablished function. Moreover, they are always synthesized in an inactive form (Girish et al. 2006).

In the present scenario, in-depth research on RIPs has been encouraged due to their miscellaneous biological involvement in viral, HIV, and microbial infections (Pizzo and di Maro 2016).

RIPs have been coupled to specific antibodies to generate immunoonjugates in cancer and HIV therapy by targeting a specific cell due to their ability to hydrolyze N-glycosidase bond (Pizzo and di Maro 2016). Anti CD4-PAP is an immunoonjugate created by combining PAP with an antibody that targets HIV-infected CD4 T-cells and prevents HIV infection (Irvin and Uckun 1992). Another example is B43-PAP (anti-CD19 pokeweed antiviral protein), an
immunotoxin made by combining B43 [an antibody-targeting CD19 antigen found on B-lineage acute lymphoblastic leukemia (ALL cells)] and PAP (Irvin and Uckun 1992). Alpha-momorcharin (0.12 nM), beta-momorcharin (0.11 nM), MAP30, balsams, isomers of luffin (a—1.64 ng/ml and b—0.84 ng/ml), ricin (814 pM), abrin (500 pM), and other plant RIPs with extremely low IC50 values have been isolated. Cell-Free Protein Synthesis (CFPS-growing in vitro) has been demonstrated to be inhibited by these RIPs (Puri et al. 2012). Despite having many RIPs, only a minority have been fully identified. Therefore, the main challenge arises in exploring and identifying some potent plant RIPs with high therapeutic efficiency and less toxicity. The available ribosome-inactivating peptides are listed in Table 5.

**Anti-carcinogenic activity of plant peptides/proteins**

One of the causes of death in recent times is the various types of cancer. Cancer caused due to genetic effects is 5-10%, but almost 90-95% of the cancers are caused due to the environment and lifestyle changes. Bioactive plant peptides can be used to cure cancer. Plant peptides prevent the proliferation of cancerous cells and cause their death-apoptosis (Hernandez-Ledesma and Hsieh 2017). A study conducted by Kannan et al. (2010) on Oryza sativa—heat stabilized defatted rice bran showed that when treated with alcalase (protease), peptide hydrolysates were produced, which are less than 5 kDa. This peptide hydrolysate was subjected to ion-exchange chromatography followed by an MTS assay. The peptide at 1000 μg/ml could show the highest inhibition for the colon and liver cancer cells for up to 84%. This study further analyzed for the amino acid composition from the peptide, and it was found that the peptide contains arginine, proline, and glutamic acid. The peptide chain was found to be glutamate-glutamine-arginine-proline-arginine, a short pentapeptide sequence. The peptide showed anti-proliferative effects on cancer cells. A peptide that prevents cancer is found in Glycine max (soybean), Triticum aestivum (wheat), Hordeum vulgare (barley) is called lunasin. Lunasin is an effective anticancer agent consisting of 43 amino acids. It has a presence of 8 aspartate residues in the C terminal; they are responsible for opposing mitosis, they play a role in the attachment of lunasin to chromatin. The amino acids arginine-glycine-aspartate are called cell adhesion motif they internalize lunasin into the cell’s nucleus. The amino acids 23–31 target the lunasin to H3–H4 histones in DNA.

In vivo mouse models were used to check the effects of lunasin on cancer cells. Lunasin was also found in Amaranthus hypochondriacus. Lunasin obtained from soybean could be taken orally as it is resistant to enzymes present in our body like pepsin and pancreatin. This property of lunasin makes it an ideal plant peptide that could cure the cancer.

The amount of lunasin found was 4.4–70.5 mg lunasin/g of protein in Glycine max, the highest among the other plants like wheat and barley (Hernandez-Ledesma et al. 2009). A study was conducted by Ma et al. (2015) on Juglans regia L. (walnut). The walnut protein was treated with different proteases, followed by purification steps to obtain the pure peptide. The peptide was further subjected to its anti-cancer activity on cells. The walnut protein hydrolyzed with papain exhibited inhibitory actions on the MCF-7 cell line (human breast cancer cell line). The peptide was found to be cysteine-threonine-leucine-glutamate-tryptophan. This peptide CTLEW induces the process of apoptosis and autophagy. The reported anti-carcinogenic proteins are listed in Table 6.

**Rational drug design**

Rational drug design is the process of designing drug molecules that bind to a target. Cyclotides are a new type of microproteins with a unique topology that includes a head-to-tail cyclized backbone structure that is further stabilised by three disulfide bonds that form a cystine knot. They are disulphide rich peptides and their basic function is plant defence. When compared to linear peptides of equal size, they have a unique molecular architecture that renders them extremely resistant to physical, chemical, and biological destruction. Apart from the conserved regions composing the cystine knot, the cyclotides are orally accessible and able to traverse cellular membranes to alter intracellular protein–protein interactions (PPIs) in vitro and in vivo. They are ideal scaffolds for numerous biotechnological applications, including drug development, because of their unique characteristics (Camarero and Campbell 2019). It does not involve trial and error like traditional drug design. The cyclotide sequences are updated on Cybase regularly. The example, plant cyclotide used is Kalakata B1, the peptide sequence is converted to cyclotide scaffold because of the cysteine knot. Graffiti of sequences from myelin oligodendrocyte glycoprotein (MOG) into kalakata B1 has been used to design drugs for multiple sclerosis (Craik and Du 2017). By applying molecular grafting of bioactive epitopes or even molecular evolution methods, it is possible to create cyclotides with unique biological properties. Cyclotides which can target a wide range of protein targets have been developed and evaluated using these methods, largely in vitro but also in animal models. Despite the early success of using the cyclotide scaffold to target specific proteins and modify their biological activity, no cyclotides have yet been tested in humans. Potential immunogenicity and oral bioavailability are two obstacles that bioactive cyclotides must overcome before entering the clinic. More research into the biopharmaceutical properties of these fascinating new micro-proteins
Table 5  List of ribosome-inactivating proteins from plants

| S. No | Plant and its part | Protein | Nature | M. Wt. (kDa) | Class of RIP | Mode of action | *IC50       | References                  |
|-------|-------------------|---------|--------|--------------|--------------|---------------|-------------|-----------------------------|
| 1     | *Momordica balsamina* (Seeds) | Balsamin | Protein | 28           | RIP-I        | 28S rRNA depurination with the liberation of RNA fragment of about 400 nucleotides | 90.6 ng/ml | Kaur et al. (2012)          |
| 2     | *Cucurbita foetidissima* (Root) | Foetidissimin | Protein | 63           | RIP-II       | 28S rRNA depurination with the liberation of RNA fragment of about 550 nucleotides | 25.9 nM   | Zhang and Halaweish (2003)  |
|       |                    | Foetidissimin II | Protein | 61           | RIP-II       | 28S rRNA depurination with the liberation of RNA fragment of about 450 nucleotides | 0.251 µM  | Zhang and Halaweish (2007)  |
| 3     | *Cucurbita texana* | Texanin (Fruit) | Protein | 29.7         | RIP-I        | 28S rRNA depurination | NA         | Zhang and Halaweish (2007)  |
|       | ME2 (Roots)       |         | Protein | 27.5         | RIP-I        | 28S rRNA depurination | NA         | Vivanco et al. (1999)       |
| 4     | *Abrus precatorius* (Seeds) | AGG     | Heterodimeric lectin | 134 | RIP-II | 28S rRNA depurination | 0.469 µg/ml | Bhutia et al. (2016)        |
|       | Abrin              |         | Homotetrameric protein | 260 | RIP-I | 28S rRNA depurination | 500 pM     | Ferreras et al. (2011)      |
| 5     | *Viscum album L.* (Green Parts) | Viscum | Heterodimeric protein | 60  | RIP-I | 28S rRNA depurination | NA         | Olsnes et al. (1982)        |
| 6     | *Amaranthus viridis L.* (Leaves) | Amaranthin | Protein | 30           | RIP-I        | 28S rRNA depurination | 25 pM      | Kwon et al. (1997)          |
| 7     | *Beta vulgaris L.* (Leaves) | Beetin-27 | Protein | 27.59        | RIP-I        | 28S rRNA depurination | 1.15 ng/ml | Iglesias et al. (2005)      |
| 8     | *Citrullus colocynthis (L.) Schrad (Seeds)* | Colocin 1 | Protein | 26.3         | RIP-I        | 28S rRNA depurination | 0.04 nM    | Bolognesi et al. (1990)     |
|       |                   | Colocin 2 | Protein | 27.98        | RIP-I        | 28S rRNA depurination | 0.063 nM   | Remi Shih et al. (1998)     |
| 9     | *Marah oreganus* (Seeds) | MOR-I   | Protein | 27.63        | RIP-I        | 28S rRNA depurination | 0.13 nM    | Puri et al. (2012)          |
|       |                   | MOR-II  | Protein | 115          | RIP-II       | 28S rRNA depurination | 0.071 nM   |                           |
| 10    | *Momordica charantia L.* (Seeds) | MCL     | Heterotetrameric lectin | 115 | RIP-II | 28S rRNA depurination | 5 µg/ml    |                           |
|       | α-momorcharin     | Protein | 28     | RIP-I        | 0.12 nM      |                           |             |                            |
|       | β-momorcharin     | Protein | 29     | RIP-I        | 0.11 nM      |                           |             |                            |
|       | MAP 30            | Protein | 30     | RIP-I        | 3.3 nM       |                           |             |                            |
|       | γ-momorcharin     | Protein | 11.5   | sRIP-I       | 55 nM        |                           |             |                            |
|       | δ-momorcharin     | Protein | 30     | RIP-I        | 0.15 nM      |                           |             |                            |
| 11    | *Trichosanthes kirilowii* Matim | TCS(GLQ223) (Seeds) | Protein | 26           | RIP-I        | 28S rRNA depurination | 0.36 ng/ml (3.7 nM) | Lee-Huang et al. (1991a); Schrot et al. (2015) |
| S. No | Plant and its part                      | Protein          | Nature       | M. Wt. (kDa) | Class of RIP | Mode of action         | *IC₅₀  | References                                      |
|-------|-----------------------------------------|------------------|--------------|--------------|---------------|------------------------|--------|------------------------------------------------|
| 1     | TAP 29 (Root tubers)                    | 29               | RIP-I        | 3.7 nM       |               |                        |        | Lee-Huang et al. (1991a)                        |
| 2     | Trichosantrhip (Seeds)                  | 10.96            | sRIP-I       | 1.6 ng/ml    |               |                        |        | Shu et al. (2009)                               |
| 3     | α-kirilowin (Seeds)                     | 28.8             | RIP-I        | 1.2–1.8 ng/ml|               |                        |        | Wong et al. (1996)                              |
| 4     | β-kirilowin (Seeds)                     | 27.5             | RIP-I        | 1.8 ng/ml    |               |                        |        |                                                 |
| 5     | Basella rubra L. (Seeds)                | Basella RIP 2a protein fraction | 30.6       | RIP-I        | NA            |                        | 1.70 ng/ml | Bolognesi et al. (1997)                        |
| 6     | Basella RIP 2b protein fraction         | 31.2             | RIP-I        | NA           |               |                        | 1.70 ng/ml |                                                 |
| 7     | Basella RIP 3                           | 31.2             | RIP-I        | 1.66 ng/ml   |               |                        |        |                                                 |
| 8     | Saponaria ocyoides L. (Seeds)           | Ocymoidin        | Protein      | 30.2         | RIP-I         | 28S rRNA depurination | 46 pM; 4.8 ng/ml | Bolognesi et al. (1995), di Massimo et al. (1997) |
| 9     | Secale cereale (Seeds)                  | RPSI (Seeds)     | Protein      | 30.1         | RIP-I         | NA                     | 0.42 µg/ml | Minami et al. (1998)                           |
| 10    | Phytolacca americana L                  | PAP (Leaves)     | Protein      | 29–30        | RIP-I         | 28S rRNA depurination | 0.29 nM | Irvin and Uckun (1992), Poyet and Hoeveler (1997) |
|       | PAP-I (Leaves)                          | 29               | RIP-I        | 3 ± 0.2 pM   |               |                        |        | Rajamohan et al. (1999)                        |
|       | PAP-II (Leaves)                         | 30               | RIP-I        | 4 ± 0.2 pM   |               |                        |        |                                                 |
|       | PAP-III (Leaves)                        | 30               | RIP-I        | 3 ± 0.2 pM   |               |                        |        |                                                 |
|       | PAP-S (Seeds)                           | 30               | RIP-I        | 36–83 nM; 1.09 |               |                        |        | Barbieri et al. (1982)                         |
|       | PAP-R (Roots)                           | 25.0             | RIP-I        | 0.05 nM      |               |                        |        | Stirpe et al. (1986)                           |
| 11    | Trichosanthes lepiniate (Root tuber)    | Trichomaglin     | Protein      | 24.6         | RIP-I         | 28S rRNA depurination | 10.1 nM | Chen et al. (1999)                             |
| 12    | Iris hollandica var. Professor Blaauw (Bulbs) | IrisRIP          | Protein      | 28           | RIP-I         | 28S rRNA depurination | 0.1–0.16 nM | Desmyter et al. (2003)                        |
|       | IrisRIP.A1                              | 29               | RIP-I        | 0.16 nM      |               |                        |        | van Damme et al. (1997)                        |
|       | IrisRIP.A2                              | 29               | RIP-I        | 0.12 nM      |               |                        |        |                                                 |
|       | IrisRIP.A3                              | 29               | RIP-I        | 0.10 nM      |               |                        |        |                                                 |
| 13    | Viscum album L. (Leaves)                | ML-I             | Heterodimeric lectin | 115            | RIP-II        | NA                     | 2.6 µg/mL | Stirpe et al. (1980)                           |
| 14    | Momordica grosvenorii (Seeds)           | Momorgrosvin     | Glycoprotein | 27.7         | RIP-I         | NA                     | 0.3 nM  | Tsang and Ng (2001)                            |
| 15    | Pisum sativum var. arvense Poir (Seeds) | α pisavins       | Protein      | 20.5         | RIP-I         | NA                     | 0.5 nM  | Lam et al. (1998)                              |
|       | β pisavins                              | 18.7             |              |              |               |                        |        |                                                 |
| 16    | Vaccaria pyramidata (Seeds)             | Pyramidatine     | Protein      | 28.0         | RIP-I         | 28S rRNA depurination | 3.6 ng/ml | di Massimo et al. (1997)                       |
Table 5 (continued)

| S. No | Plant and its part | Protein | Nature       | M. Wt. (kDa) | Class of RIP | Mode of action                  | *IC$_{50}$  | References                        |
|-------|--------------------|---------|--------------|--------------|--------------|---------------------------------|------------|-----------------------------------|
| 22    | *Cinnamomum porrec-<br>tum (Seeds)* | Parrettin | Glycoproteins | 64.5         | RIP-II       | 28S rRNA depurination           | 0.11 µM    | Li et al. (1996)                  |
| 23    | *Cicer arietinum (Seeds)* | CLAP    | Protein      | 18           | –            | NA                              | 20 µM      | Ye and Ng (2002a)                |
| 24    | *Phaseolus mungo (Seeds)* | Mungin  | Protein      | 18           | –            | NA                              | 24 µM      | Ye and Ng (2000)                 |
| 25    | *Adzukia angularia (Seeds)* | Fraction AB2 | Peptide | 5            | –            | NA                              | 11 µM      | Ye and Ng (2001)                 |
| 26    | *Phaseolus vulgaris (Seeds)* | Fraction PTA2c | Peptide | 5            | –            | NA                              | 9 µM       | Ye and Ng (2001)                 |
| 27    | *Dianthus caryophyllus (Leaves)* | DAPS 30 | Protein      | 30           | RIP-I        | 28S rRNA depurination           | 3.4 nM     | Lee-Huang et al. (1991b)         |
| 28    | *Gelonium multiflorum (Seeds)* | GAP 31  | Protein      | 31           | RIP-I        | 28S rRNA depurination           | 4.1 nM     | Lee-Huang et al. (1991b)         |
| 29    | *Asparagus officinali (Seeds)* | Asparin 1 | Protein     | 30.5         | RIP-I        | NA                              | 0.27 nM    | Bolognesi et al. (1990)          |
|       |                    | Asparin 2 | -            | 29.8         | -            | -                               | 0.15 nM    | Kishida et al. (1983)            |
| 30    | *Luffa cylindriaRoem (Seeds)* | Luffin  | Protein      | 26           | RIP-I        | NA                              | 0.42 ng/ml | Ng et al. (1992b); Schrot et al. (2015) |
|       |                    | Luffin a | -            | 28           | -            | -                               | 1.64 ng/ml | Ng et al. (1992b); Schrot et al. (2015) |
|       |                    | Luffin b | -            | 29           | -            | -                               | 0.84 ng/ml | Ng et al. (1992b); Schrot et al. (2015) |
| 31    | *Lychnis chalcedonica (Seeds)* | Lychnin | Protein      | 26.6         | RIP-I        | NA                              | 0.17 nM    | Bolognesi et al. (1990)          |
| 32    | *Manihot palmata (Seeds)* | Mapalmin | Protein      | 32.3         | RIP-I        | NA                              | 0.05 nM    | Bolognesi et al. (1990)          |
| 33    | *Bryonia dioica* | Bryodin-L (Leaves) | Protein | 28.8         | RIP-I        | NA                              | 0.09 nM    | Bolognesi et al. (1990)          |
|       |                    | Bryodin (Roots) | -            | 30           | -            | -                               | 0.12 nM    | Bolognesi et al. (1990)          |
| 34    | *Ricinus communis.L (Seeds)* | Ricin D = Ricin | Glycoprotein | 62.8         | RIP-II       | 28S rRNA depurination           | 5.5 ng/ml; 814 pM | Battelli et al. (1997), Endo and Tsurugi (1987), Schrot et al. (2015), Wei and Koh (1978) |
|       |                    | Ricin E  | -            | 64           | -            | -                               | NA         | Schrot et al. (2015)            |
|       |                    | RCA     | -            | 118–130      | -            | -                               | NA         | Schrot et al. (2015)            |
| 35    | *Ricinus communis.L USA (Seeds)* | Ricin 1 | Glycoprotein | 66           | RIP-II       | 28S rRNA depurination           | NA         | Schrot et al. (2015)            |
|       |                    | Ricin 2  | -            | -            | -            | -                               | NA         | Schrot et al. (2015)            |
|       |                    | Ricin 3  | -            | -            | -            | -                               | NA         | Schrot et al. (2015)            |
| S. No | Plant and its part | Protein | Nature | M. Wt. (kDa) | Class of RIP | Mode of action | *IC$_{50}$ | References |
|-------|-------------------|---------|--------|--------------|--------------|----------------|------------|------------|
| 36    | *Ricinus communis*, India (Seeds) | Ricin I | Glycoprotein | 64 | RIP-II | 28S rRNA depurination | NA | |
|       |                   | Ricin II | | | | | | |
|       |                   | Ricin III | | | | | | |
| 37    | *Trichosanthes cucumeroides* (Set.) Maxim (Root tubers) | β-TCS | Protein | 28 | RIP-I | 28S rRNA depurination | 2.8 ng/ml; 0.1 nM | Ng et al. (1992a); No et al. (1991); Yeung and Li (1987) |
| 38    | *Saponaria officinalis* L | Saporin-L1 (Leaves) | Protein | 31.6 | RIP-I | 28S rRNA depurination | 0.25 nM | Ferreras et al. (1993) |
|       |                   | Saporin-L2 (Leaves) | | 31.6 | | 0.54 nM | | |
|       |                   | Saporin-R1 (Roots) | | 30.2 | | 0.86 nM | | |
|       |                   | Saporin-R2 (Roots) | | 30.9 | | 0.47 nM | | |
|       |                   | Saporin-R3 (Roots) | | 30.9 | | 0.48 nM | | |
|       |                   | Saporin-S5 (Seeds) | | 30.9 | | 0.05 nM | | |
|       |                   | Saporin-S6 (Seeds) | | 31.6 | | 0.06 nM | | |
| 39    | *Phaseolus vulgaris* (Seeds) | Vulgarinin | Peptide | 7 | – | NA | 13 μM | Wong and Ng (2005c) |
| 40    | *Adenia digitata* (Roots) | Modeccin | Protein | 57–63 | RIP-II | 28S rRNA depurination | 4 μg/ml | Olsnes et al. (1978); Schrot et al. (2015) |
|       |                   | Modeccin 6B | | 57 | | 0.31 μg/ml | | Barbieri et al. (1980) |
| 41    | *Panax ginseng* (Roots) | Panaxagin | Homodimeric protein | 53 | – | NA | 0.28 nM | Ng and Wang (2001) |
| 42    | *Allium tuberosum* (Shoot) | Fraction MS3 | Protein | 36 | – | NA | 850 nM | Lam et al. (2000) |

*IC$_{50}$ Concentration causing 50% inhibition, ND Not determined, NA Not available, *CAP30* *Chenopodium album* antiviral RIP, *RPSI* Rye protein synthesis inhibitor, *PAP* Pokeweed anti-viral protein, *IrisRIP = IRIP* Type-1 ribosome-inactivating protein from iris bulbs, *CLAP* Chickpea cyclophilin-like antifungal protein, Fraction AB2 Red bean antifungal peptide, Fraction PTA2c Pinto bean antifungal peptide, *DAPs 30* Dianthus anti-HIV proteins, *GAP 31* Gelonium anti-HIV protein, *RCA* *Ricinus communis* agglutinin, TAP 29 Trichosanthes anti-HIV protein, β-TCS β-trichosanthin
| S. No | Plant and its part | Protein | Nature | Sequence | Mode of action | M. Wt. (kDa) | *IC\textsubscript{50} | References |
|-------|---------------------|---------|--------|----------|----------------|-------------|-------------|------------|
| 1     | *Acacia confuse* (Seeds) | Acaconin | Protein | DPLLDFPGNEVEAS-RAYVVSVIRGAG | Prevents the growth of human hepatoma cells and leukemia cells | 32 | 128±9 µM | Lam and Ng (2010) |
| 2     | *Clausena lansium* (Lour) (Seeds) | CLTI | Homodimeric protein | DPLLDFPGNEVEAS-RAYVVSVIRGAG | Prevents the growth of human hepatoma cells and leukemia cells | 54 | 100 µM | Ng et al. (2003) |
| 3     | *Momordica charantia* (Seeds) | BG-4 | Peptide | RDSDCLAQCIYVGHC | Apoptosis of human colon cancer cells | 4 | NA | Dia and Krishnan (2016) |
|       |                     |         |        |             |                |             | 134.4 µg/ml | |
|       |                     |         |        |             |                |             | 217.0 µg/ml | |
|       |                     |         |        |             |                |             | 28.6 µM | |
|       |                     |         |        |             |                |             | 6.9 µM | |
| 4     | *Castanopsis chinensis* (Seeds) | CCL | Homotetrameric lectin | NFEETILGSK | Prevents growth of HepG2 cells | 120 | NA | Wong et al. (2008) |
| 5     | *Phaseolus lunatus* (Seeds) | Lunatin | Peptide | KTCENLADTRGPGC-FATSNC | Inhibits growth of MCF-7, breast cancer cell line | 7 | 5.71 µM | Wong and Ng (2005a) |
| 6     | *Vigna sesquipedalis* (Seeds) | Sesquin | Peptide | KTCENLADTY | Anti-tumour activity | 7 | NA | Wong and Ng (2005b) |
| 7     | *Phaseolus coccineus cv. ‘Major’* (Seeds) | Coccin | Peptide | KQTENLADTY | Prevents proliferation in leukemia cell lines | 7 | 30 µM | Ngai and Ng (2004) |
|       |                     |         |        |             |                |             | 40 µM | |
| 8     | *Arachis hypogaea* (Seeds) | Hypotin | Protein | CDVGSVISALFE-ALQKRRN | Anti-proliferative activity | 30.4 | 296 µg/ml | Wang et al. (2007) |
| 9     | *Cicer arietinum* (Seeds) | C-25 | Lectin | TKTGYINAADF | Anti-proliferative activity | 25 | 37.5 µg/ml | Kumar et al. (2014) |
| 10    | *Corydalis cava* (Tubers) | Fraction 18 | Protein | – | Prevents the growth of human carcinoma cells | 30 | NA | Nawrot et al. (2010) |
| 11    | *Arisaema tortuosum* Schott (Tubers) | ATL | Homotetrameric lectin | – | – | 54 | NA | Dhuna et al. (2005) |
Table 6 (continued)

| S. No | Plant and its part | Protein | Nature | Sequence | Mode of action | M. Wt. (kDa) | IC50 | References |
|-------|-------------------|---------|--------|----------|---------------|-------------|------|------------|
| 12    | *Phaseolus vulgaris*<br/> *cv. Blue tiger king*<br/> (Seeds) | BTKL    | Dimeric lectin | –        | –             | 60          | 35.2 ± 2.7 µM | Fang et al. (2011b) |
|       |                   |         |        |          |               |             | 347.9 ± 24.5 µM |     |
|       |                   |         |        |          |               |             | 494.6 ± 70.4 µM |     |
| 13    | *Canavalia ensiformis*<br/> (Seeds) | Con A   | Homotetraeric lectin | –        | Anti-hepatoma effect | 104 | 5 µg/ml | Lei and Chang (2009), Liu et al. (2009) |
|       |                   |         |        |          |               |             | 10 µg/ml |     |
|       |                   |         |        |          |               |             | 20 µg/ml |     |
|       |                   |         |        |          |               |             | NA      |     |
| 14    | *Withania somnifera*<br/> (Fruit) | Asparginase | Homodimeric protein | –        | Anti-tumour activity | 72 ± 0.5 | 1.45 ± 0.05 IU/ml | Oza et al. (2010) |
| 15    | *Glycine max* (Seeds) | BBI     | Peptide | –        | Colorectal chemopreventive agents | 8 | 32 to 73 µM | Clemente and del Carmen Arques (2014); Kennedy (1998) |
|       |                   |         |        |          |               |             | NA      |     |
|       |                   | IBB1    | Protein | DDESSKPCCDQCACIK<br/> SNPPQCRCSDM<br/> RLNSCHSACKSCICAL<br/> SYPACFCVDITDFCY<br/> EPCKPSEDHKEN | Colorectal chemopreventive agents | 10–12 | 39.9 ± 2.3 µM | Clemente et al. (2010) |
|       |                   | IBBD2   | Protein | SDQSSYDDDEYSKPC<br/> CDLCMCTRMPPQC<br/> SCEDIRLNSCHSDCK<br/> SCMTQSDQPPQR<br/> CLDTNDFCYKPK<br/> SRDD | colorectal chemopreventive agents | 10–12 | 48.3 ± 3.5 µM |     |
| 16    | *Abrus precatorius*<br/> (Seeds) | Abrin   | Homotetrameric protein | –        | –             | 260         | 3.70 pM | Lin et al. (1971); Olesen and Pihl (1973) |
|       |                   | AGG     | Heterodimeric glyco-protein | –        | –             | 134         | NA      | Bhutia et al. (2016); Mukhopadhyay et al. (2014) |
| 17    | *Trichosanthes kirilowii* (Root Tuber) | TCS     | Protein | 26–27    | –             | 31.6 µM     |        | Fang et al. (2012c) |
|       |                   |         |        |          |               |             | 20.5 µM |     |
|       |                   |         |        |          |               |             | 130 µM  |     |
|       |                   |         |        |          |               |             | 28.6 µM |     |
| S. No | Plant and its part                     | Protein       | Nature            | Sequence | Mode of action | M. Wt. (kDa) | *IC$_{50}$ | References                        |
|-------|---------------------------------------|---------------|-------------------|----------|----------------|--------------|-----------|-----------------------------------|
| 18    | *Gynura procumbens* (Lour.) Merr. (Leaves) | SN-F11/12     | Mixture of proteins |          |                | 25           | 3.8 µg/ml | Tsao et al. (1986)               |
| 19    | *Allium sativum* (Bulbs)              | Alliumin      | Protein           |          |                | 13           | 8.33 µM   | Xia and Ng (2005)                |
| 20    | *Cucurbita foetidissima* (Roots)      | Foetidissimin II | Proteins          |          |                | 61           | 70 nM     | Zhang and Halaweish (2007)       |
| 21    | *Viola arvensis* (Whole plant)        | Varv A        | Macrocyclic peptides |          |                | 2.87         | 3.56 µM   | Lindholm et al. (2002)           |
|       |                                       | Varv F        | Macrocyclic peptides |          |                | 2.95         |          | 1.34 µM 4.88 µM 11.03 µM 3.24 µM 3.19 µM 6.35 µM 7.13 µM 7.49 µM 7.07 µM 5.90 µM 6.31 µM NA | | |
| 22    | *Viola odorata* (Whole plant)         | Cycloviolacin O2 | Macrocyclic peptides |          |                | 3.14         | 0.11 µM   | Lindholm et al. (2002)           |
|       |                                       |               |                   |          |                |              | 0.12 µM 0.26 µM 0.12 µM 0.12 µM 0.10 µM 1.32 µM | | |
| 23    | *Viola biflora* (Aerial parts)        | Vibi D        | Macrocyclic peptides |          |                | 2.9          | > 30 µM    | Herrmann et al. (2008)           |
|       |                                       | Vibi E        |                   |          |                | 3.08         | 3.2 µM    |                                   |
|       |                                       | Vibi G        |                   |          |                | 3.2          | 0.96 µM   |                                   |
|       |                                       | Vibi H        |                   |          |                | 3.27         | 1.6 µM    |                                   |
| S. No | Plant and its part | Protein | Nature          | Sequence | Mode of action | M. Wt. (kDa) | *IC₅₀ | References |
|-------|--------------------|---------|-----------------|----------|----------------|--------------|--------|------------|
| 24    | Viola philippica   | Vphi A  | Macrocyclic peptides |          |                | 3.17         | 4.91 ± 0.04 µM | He et al. (2011) |
|       | (Whole plant)      | Vphi B  |                 |          |                | 2.98         | NA     |            |
|       |                    | Vphi C  |                 |          |                | 3.05         | NA     |            |
|       |                    | Vphi D  |                 |          |                | 3.08         | 2.51 ± 0.03 µM | He et al. (2011) |
|       |                    | Vphi E  |                 |          |                | 3.15         | 2.51 ± 0.03 µM |            |
|       |                    | Vphi F  |                 |          |                | 3.14         | 1.03 ± 0.03 µM |            |
|       |                    | Vphi G  |                 |          |                | 3.17         | 1.03 ± 0.03 µM |            |
|       |                    | Vphi H  |                 |          |                | 3.09         | NA     |            |
|       |                    | Viba 15 |                 |          |                | 2.86         | 1.32 ± 0.15 µM |            |
|       |                    | Viba 17 |                 |          |                | 2.84         | 1.32 ± 0.15 µM |            |
|       |                    | Varv A  |                 |          |                | 2.87         | 1.32 ± 0.15 µM |            |
|       |                    | Kalata B1 |              |          |                | 2.89         | 1.32 ± 0.15 µM |            |
| 25    | Viola labidorica   | Vila A  | Macrocyclic peptides |        |                | 3.16         | 7.08 µg/ml | Tang et al. (2010a) |
|       | (Whole Plant)      |         |                 |          |                |             | 5.13 µg/ml |            |
|       |                    |         |                 |          |                |             | > 10 µg/ml |            |
|       |                    |         |                 |          |                |             | 5.08 µg/ml |            |
| S. No | Plant and its part       | Protein | Nature                  | Sequence | Mode of action | M. Wt. (kDa) | \(^{*}IC_{50}\) | References                   |
|-------|--------------------------|---------|-------------------------|----------|----------------|--------------|----------------|-----------------------------|
| 5     | Viola B                  |         | Macrocyclic peptides    | 5.80 µg/ml | > 10 µg/ml     | 3.16         | 34.65 µg/ml    |                             |                             |
| 6     | Viola D                  |         | Macrocyclic peptides    | 8.25 µg/ml | > 10 µg/ml     | 2.94         | 49.59 µg/ml    |                             |                             |
| 7     | Varv D                   |         | Macrocyclic peptides    | 6.34 µg/ml | > 10 µg/ml     | 2.87         | 46.62 µg/ml    |                             |                             |
| 26    | Psychotria leptothyrsa (Whole Plant) | Psyle A | Macrocyclic peptides    | 5.80 µg/ml | > 10 µg/ml     | 2.91         | 26 µM          | Gerlach et al. (2010)       |                             |
|       |                          |         |                         |          |                |              |                |                             |                             |
|       |                          | Psyle B | Macrocyclic peptides    | 5.80 µg/ml | > 10 µg/ml     | .01          | NA             | NA              |                             |
|       |                          | Psyle C | Linear cyclotide        | 5.80 µg/ml | > 10 µg/ml     | 2.84         | 3.5 µM         | NA              |                             |
|       |                          | Psyle D | Macrocyclic peptides    | 5.80 µg/ml | > 10 µg/ml     | 3.25         | NA             | NA              |                             |
|       |                          | Psyle E | Macrocyclic peptides    | 5.80 µg/ml | > 10 µg/ml     | 3.25         | 0.76 µM        | NA              |                             |
|       |                          | Psyle F | Macrocyclic peptides    | 5.80 µg/ml | > 10 µg/ml     | 3.21         | NA             | NA              |                             |
| 27    | Viola abyssinica (Whole Plant) | Vaby A | Macrocyclic peptides    | 5.80 µg/ml | > 10 µg/ml     | 2.86         | 7.6 µM         | Yeshak et al. (2011)       |                             |
|       |                          | Vaby D  | Macrocyclic peptides    | 5.80 µg/ml | > 10 µg/ml     | 3.06         | 2.8 µM         |                             |                             |
| 28    | Viola tricolor (Whole Plant) | Varv A | Macrocyclic peptides    | 5.80 µg/ml | > 10 µg/ml     | 2.87         | 3 µM           | Tang et al. (2010b)         |                             |
|       |                          |         |                         |          |                |              | 6 µM           |                             |                             |
| S. No | Plant and its part | Protein Nature | Mode of action | M. Wt. (kDa) | *IC$_{50}$ | References |
|-------|--------------------|----------------|----------------|--------------|------------|------------|
| 37    | 18 µg/ml           | > 10 µg/ml     | > 10 µg/ml     | > 10 µg/ml   | > 10 µg/ml |            |
| 38    | 62 µg/ml           | > 10 µg/ml     | > 10 µg/ml     | > 10 µg/ml   | > 10 µg/ml |            |
| 39    | 84 µg/ml           | > 10 µg/ml     | > 10 µg/ml     | > 10 µg/ml   | > 10 µg/ml |            |
| 40    | 49 µg/ml           | > 10 µg/ml     | > 10 µg/ml     | > 10 µg/ml   | > 10 µg/ml |            |
| 41    | 70 µg/ml           | > 10 µg/ml     | > 10 µg/ml     | > 10 µg/ml   | > 10 µg/ml |            |
| 42    | 54 µg/ml           | > 10 µg/ml     | > 10 µg/ml     | > 10 µg/ml   | > 10 µg/ml |            |
| 43    | 53 µg/ml           | > 10 µg/ml     | > 10 µg/ml     | > 10 µg/ml   | > 10 µg/ml |            |
| S. No | Plant and its part | Protein | Nature       | Sequence | Mode of action | M. Wt. (kDa) | *IC₅₀ | References |
|-------|---------------------|---------|--------------|----------|----------------|--------------|-------|------------|
|       | Varv Hm             | Macrocyclic peptides | 3.06 | > 10 µg/ml | 74.39 µg/ml | > 10 µg/ml | > 10 µg/ml | > 10 µg/ml | > 10 µg/ml | > 10 µg/ml | NA |
|       |                      |          |              |          | > 10 µg/ml     |              |       |            |
|       | Vitri A             | Macrocyclic peptides | 3.15 | 3.90 µg/ml | 4.94 µg/ml | 3.07 µg/ml | 3.69 µg/ml | NA | 6.03 µg/ml | NA |
|       |                      |          |              |          | > 10 µg/ml     |              |       |            |
|       | Vitri B             | Macrocyclic peptides | 2.87 | > 10 µg/ml | 45.21 µg/ml | > 10 µg/ml | > 10 µg/ml | > 10 µg/ml | NA | 45.21 µg/ml | NA |
|       |                      |          |              |          | > 10 µg/ml     |              |       |            |
|       | Vitri C             | Macrocyclic peptides | 2.96 | > 10 µg/ml | 46.96 µg/ml | > 10 µg/ml | > 10 µg/ml | > 10 µg/ml | NA | 46.96 µg/ml | NA |
|       |                      |          |              |          | > 10 µg/ml     |              |       |            |
|       | Vitri D             | Macrocyclic peptides | 3.04 | > 10 µg/ml | 51.65 µg/ml | > 10 µg/ml | > 10 µg/ml | > 10 µg/ml | NA | 51.65 µg/ml | NA |
|       |                      |          |              |          | > 10 µg/ml     |              |       |            |
|       | Vitri E             | Macrocyclic peptides | 2.92 | > 10 µg/ml |          |              |       |            |
| S. No | Plant and its part     | Protein   | Nature        | Sequence | Mode of action | M. Wt. (kDa) | *IC$_{50}$ | References         |
|-------|------------------------|-----------|---------------|----------|----------------|--------------|------------|-------------------|
| 29    | *Vicia faba* cv. Giza 843 (Seeds) | VFTI-G1   | Protein       | 15       | > 3.33 µM      | 54.39 µg/ml  | > 10 µg/ml | Fang et al. (2011a) |
| 30    | *Asparagus officinalis* (Seeds) | Asparin 1 | Protein       | 29.7     | > 3.33 µM      | 5.36 µg/ml   | > 10 µg/ml | Bolognesi et al. (1990) |
|       |                        | Asparin 2 | Protein       | 28.1     | > 3.33 µM      | 3.44 µg/ml   | > 10 µg/ml |                   |
| 31    | *Citrullus colocynthis* (Seeds) | Colocin 1 | Glycoprotein  | 20.4     | > 3.33 µM      | 2.74 µg/ml   | > 10 µg/ml |                   |
|       |                        | Colocin 2 | Glycoprotein  | 19.5     | 1.41 µM        | 6.31 µg/ml   | > 10 µg/ml |                   |
| 32    | *Lychnis chalcedonica* (Seeds) | Lychnin   | Glycoprotein  | 20.0     | > 3.33 µM      | NA          | NA        |                   |
| S. No | Plant and its part | Protein | Nature       | Sequence | Mode of action | M. Wt. (kDa) | \( {IC}_{50} \) References |
|-------|-------------------|---------|--------------|----------|--------------|-------------|-------------------|
| 33    | *Manihot palmata* (Seeds) | Mapalmin | Glycoprotein |          | 26.9         | 2.11 µM     | > 3.33 µM       |
|       |                   |         |              |          |              | 0.03 µM     |                   |
|       |                   |         |              |          |              | 1.53 µM     |                   |
|       |                   |         |              |          |              | 0.33 µM     |                   |
| 34    | *Bryonia dioica* | Bryodin-L (Leaves) | Glycoprotein |          | 27.3         | 1.68 µM     | > 3.33 µM       |
|       |                   |         |              |          |              | 0.03 µM     |                   |
|       |                   |         |              |          |              | 1.64 µM     |                   |
|       |                   |         |              |          |              | 0.08 µM     |                   |
|       |                   | Bryodin (Roots) | Glycoprotein |          | 30           | 0.77 µM     |                         |
|       |                   |         |              |          |              | 0.05 µM     |                         |
|       |                   |         |              |          |              | > 3.33 µM   |                         |
|       |                   |         |              |          |              | NA          | Stirpe et al. (1986) |
| 35    | *Bauhinia variegata* var. variegate (Seeds) | BvvL | Homodimeric lectin |          | 64           | 1.4 µM      | Chan and Ng (2015)   |
|       | *Bauhinia variegata* (Seeds) | BG2 | Homodimeric lectin |          |              | 1.4 µM      | Lin and Ng (2008)     |
|       |                   |         |              |          |              | 0.18 µM     | Gondim et al. (2017)  |
|       | *Dioclea lasiocarpa* (Seeds) | DlasiL | Homotetrameric lectin |          |              | 52 ± 2 nM   | Gondim et al. (2017)  |
| 37    | *Lens culinaris* (Seeds) | Bowman-Birk Isoinhibitor | Peptide |          | 7.5           | 224 ± 10 nM | Caccialupi et al. (2010) |
| 38    | *Pisum Sativum* (Seeds) | TII B | Peptide |          | 7.9           | 275 ± 4 nM  | Clemente et al. (2012) |
| 39    | *Canavalia brasiliensis* (Seeds) | ConBr | Lectin |          | 30           | 167 ± 1 nM  | Grangeiro et al. (1997) |
| S. No | Plant and its part | Protein | Nature     | Sequence | Mode of action | M. Wt. (kDa) | *IC<sub>50</sub>     | References                  |
|-------|--------------------|---------|------------|----------|---------------|--------------|----------------|-----------------------------|
| 40    | *Canavalia maritima* (Seeds) | ConM    | Tetrameric lectin | 102      | 95 ± 14 nM     | 1146 ± 24 nM | 529 ± 8 nM | 67 ± 2 nM | Delatorre et al. (2006) |
| 41    | *Dioclea sclerocarpa* (Seeds) | DscLrL  | Lectin      |          | Anti-cancer   | 64 ± 2 nM   | 102 ± 8 nM | 1250 ± 9 nM | Gondim et al. (2017) |
| 42    | *Aspidistra elatior Blume* (Rhizomes) | AEL     | Heterotetramer lectin | 56       | NA            | 141 ± 4 nM   | 264 ± 1 nM |               | Xu et al. (2007) |
| 43    | *Soybean* (Cotyledon) | Lunasin | Peptide    | MTKFILTIS LLIFCIAHTCS | 5.5 | 181 µM | 16 µM | 25 nM | Hernandez-Ledesma et al. (2013) |
| 44    | *Saponaria officinalis L* | Saporin-L1 (Leaves) | Protein | MKSWMHVT WLIILQTVT | 31.6 | > 3300 nM | 120 nM | 13 nM | Ferreras et al. (1993) |
|       |                    | Saporin-L2 (Leaves) | Protein | –        | 31.6 | > 3300 nM | 150 nM       |               |                     |
|       |                    | Saporin-R1 (Roots) | Protein | –        | 30.2 | 340 nM | 490 nM | 76 nM |                     |
|       |                    | Saporin-R2 (Roots) | Protein | –        | 30.9 | 170 nM | 230 nM | 33 nM |                     |
|       |                    | Saporin-R3 (Roots) | Protein | –        | 30.9 | 3200 nM | 84 nM | 34 nM |                     |
|       |                    | Saporin-S5 (Seeds) | Protein | –        | 30.9 | 420 nM | 7 nM |   |                     |
| S. No | Plant and its part              | Protein       | Nature        | Sequence | Mode of action | M. Wt. (kDa) | *IC_{50} | References          |
|-------|---------------------------------|---------------|---------------|----------|----------------|--------------|---------|---------------------|
| 45    | *Ricinus communis* (Seeds)      | Saporin-S6    | Protein –     | 31.6     | 2 nM           | 310 nM       | 18 nM   | 6 nM                |
| 46    | *Basella rubra L.* (Seeds)      | Ricin         | Protein       | 64       | 34.1 ng/ml     | Trung et al. (2016) |
|       |                                  | Basella RIP 2 | Mixture of two proteins | 30.6–31.2 | 63.7 ± 15.6 nM | Bolognesi et al. (1997) |
|       |                                  | Basella RIP 3 | Protein       | 31.2     | 43.8 ± 9.2 nM  |              | 166 ± 24 nM | 16.6 ± 3.7 nM         |
|       |                                  |              |              |          |                |              | 169 ± 87 nM | 353 ± 5.7 nM          |
|       |                                  |              |              |          |                |              | 30.6–31.2 | 63.7 ± 15.6 nM         |
| 47    | *Vaccaria pyramidata* (Seeds)   | Pyramidatine  | Protein       | 28.0     | 6.3 nM         | Bolognesi et al. (1995) |
| 48    | *Saponaria ocymoides* L. (Seeds) | Ocymoidin     | Protein       | 30.2     | 11.7 nM        |              | 179 nM | 142 nM |
|       |                                  |              |              |          |                |              | 5.7 nM | 4.3 nM |
|       |                                  |              |              |          |                |              | 493 nM | > 3330 nM          |
| 49    | *Viscum album* L. var. coloratum (Arial parts) | VCA          | Heterodimeric lectin – | Anti-tumour | 60 | Han et al. (2015) |
| 50    | *Viscum album* L. (N.A.)        | ML-I         | Heterodimeric lectin | 115      | 125 ng/ml | 60 | 125 ng/ml |
|       |                                  | ML-II        | Heterodimeric lectin |          | NA     | 7 ng/ml | Fnnz et al. (1981) |
| S. No | Plant and its part | Protein | Nature | Sequence | Mode of action | M. Wt. (kDa) | *IC<sub>50</sub> | References |
|-------|--------------------|---------|--------|----------|----------------|--------------|-------------|------------|
| 51    | *Dianthus superbus*-var longicalycinus (Whole Plant) | Longicalycinin A | Cyclic peptide | Cyclo(Gly1–Phe2–Tyr3–Pro1–Phe5–| Cytotoxic to HepG2 cancer cell line | 50 | 6.11 | 13.52 µg/ml | Hsieh et al. (2005) |
| 52    | *Phaseolus vulgaris* (Seeds) | Vulgarinin | Peptide | K T CENLADTYKG CFTS G GD | Inhibition of proliferation in leukemia cell lines | 7 | NA | Wong and Ng (2005c) |
| 53    | *Brassica juncea* var. *Integrifolia* (Seeds) | Juncin | Protein | – | – | 18.9 | 5.6 µM | Kwon et al. (1997) |
| 54    | *Peganum harmala* (Seeds) | PHP | Homodimeric protein | ITCPQVTQSLAP-CVPYLISG | Anti-proliferative activity against cancer cells | 18 | 0.7 µM | Ma et al. (2013) |
| 55    | *Allium tuberosum* (Shoot) | Fraction MS3 | Protein | – | – | 36 | 2.74 µM, 3.13 µM, 1.47 µM | Lam et al. (2000) |
| 56    | *Zingiber officinalis* (Rhizome) | G-24 | Protein | – | Inhibition of human oral cancer cell line | 24 | NA | Gill et al. (2012) |

*IC<sub>50</sub>* Concentration causing 50% inhibition, *ND* Not determined, *NA* Not available, *CLTI* *Clausena lanzium* trypsin inhibitor, *VFTI-G1* Bowman birk type trypsin inhibitor, *BG-4* Bitter gourd-4, *MAP 30* Momordica anti-human immunodeficiency virus protein, *ML* *Momordica charantia* lectin, *α-MMC* α-Momorcharin, *CCL* *Castanopsis chinensis* lectin, *ATL* *Arisaema tortuosum* lectin, *BTKL* Blue Tiger King Lectin, *Con A* *Concanavalin A*, *BBI* Bowman birk inhibitor, *IBB1* and *IBB2* Bowman birk isoinhibitors, *TCS* *Trichosanthin* or *Tin Hua Fen* or *GLQ223*, *BvvL* *Bauhinia variegate* var *variegata* lectin, *DsclerL* *Dioclea sclerocarpa* lectin, *VCA* *Viscum album* L. var *coloratum* agglutinin, *ML-I,II,III* Mistletoe lectin-I,II,III, *PHP* *Peganum harmala* protein, *AEL* *Aspidistra elatior* Blume lectin, *AGG* *Abrus agglutinin*
is expected to be released soon (Camarero and Campbell 2019).

**Conclusion**

Finally, this review encapsulates the therapeutic plant peptides and their prospective applications. They can serve as future treatments that are both unique and effective. Although many plant peptides have been explored for therapeutic applications, only a handful have progressed to the next stages. Usually, drug development constitutes in vitro examinations, in vivo corroboration and clinical trial review. Regrettably, almost all the research involving protein therapies reaches a dead-end in vitro, with only a handful of them being marketed as medicine. Various strategies have been applied to overcome such disadvantages (low bioavailability, high toxicity). One such strategy is bioconjugation and it has improved target selectivity, lower toxicity, and enhanced retention time with a regulated release in the target tissue. As these intricate component systems become more ubiquitous, research into bioconjugate treatments should become more focused due to their peculiarity in contrast to single-molecule drug organization. New formulation strategies have to be developed to design new drug candidates and bring out the peptide's full potential. To summarise, substantial research into medicinal plant proteome could identify novel plant-based peptide drugs. Many therapies involving proteins could be discovered due to research in this approach. Plant-derived peptide therapeutics is still the primary source of bioactive compounds worldwide.

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**Declarations**

**Conflict of interest** The authors have no conflicts of interest to declare that are relevant to the content of this article.

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