|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Virulence factors** | **Organisms** | **Role**  | **Inhibitors** | **References** |
| Proteinases | *C. albicans* | Hydrolytic enzyme | Pepstatin A, saquinavir, indinavirHuman domain antibodies | [152,153] |
| Phospholipases | *C. albicans, C. neoformans, Aspergillus flavus* | Hydrolytic enzyme | Alexidine dihydrochloride,1,12 bis-(tributylphosphonium)-dodecane dibromide | [64] |
| Haemolysin | *C. albicans* | Hydrolytic enzyme | cationic lipo-benzamide compound C9M | [154] |
| Candidalysin | *C. albicans* | Hydrolytic enzyme | cis-2-dodecenoic acid | [155] |
| Elastase  | *Trichophyton mentagrophytes, Candida* spp | Hydrolytic enzyme | Aliphatic aldehydes | [68] |
|  |  |  |  |  |
| Glyoxilate cycle | *C. albicans* | Metabolic pathways | Caffeic acid, rosmarinic acid and apigenin  | [156] |
| Inositol phosphorylceramide synthase (IPC1) | *C. neoformans, Candida* spp, *Aspergillus* spp | Metabolic pathways | Aureobasidin A, khafrefungin | [157] |
| Isocitratelyase (ICL) | *C. albicans* | Metabolic pathways | 3-nitropropionate, 3-bromopyruvate, mycenon, mohangamide A and mohangamide B | [138,139] |
| Target of Rapamycin (TOR) signaling pathway | *Saccharomyces cerevisae* | Metabolic pathways | Small molecule CID 3528206 | [158] |
| Calcineurin | *C. albicans, C. neoformans* | Metabolic pathways | Tacrolimus, cyclosporin A | [135] |
| Hyphal formation | *Candida* spp, *C. neoformans* | Morphogenesis | Saponins | [88] |
| Adhesion, morphogenesis, biofilm | *C. albicans* | Ras1-cAMP-Efg1 pathway | Magnolol and honokiol | [159] |
| Biofilm | *Candida* spp | drug-resistance  | Farnesol, Diazaspiro-decane structural analogs, cationic lipo-benzamide compound C9M | [100, 112, 154]  |



Need for newer antifungal drug discovery by

* Targeting pathogenicity of fungi especially in *Candida albicans*
* Prominent Virulence factors being targeted are extracellular hydrolytic enzymes, adherence, morphogenesis, and biofilm formation
* Targeting metabolic pathways or transcription factors controlling these virulence determinants

Use of molecular approaches

various virulence factors in fungi and their known inhibitors

Problems associated with currently available antifungals

* Drug resistance
* Host toxicity
* Cost measures
* Drug efficacy