

## Treatment of *Herpes genitalis* and *Herpes zoster* with *Clinacanthus nutans*

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*Herpes genitalis* and *Herpes zoster* are caused by the viruses *Herpes simplex* type 2 (HSV-2) and Varicella-Zoster (VZV) both belonging to the family Herpesviridae. The diseases are quite common throughout the world, and their prevalence is expected to increase with the increasing prevalence of the immunocompromised hosts. Although mortality from the diseases is extremely low, nearly all infected patients suffer during a symptomatic episode and the diseases lead to a great deal of economic loss due to the high cost of anti-viral drugs. The current standard therapy for *Herpes genitalis* and *Herpes zoster* is acyclovir. Acyclovir is indicated in the treatment of primary HSV-2 infection, disseminated diseases and the diseases in the immunocompromised hosts.

*Clinacanthus nutans*, Lindau is a medicinal plant easily grown throughout Thailand. It has long been claimed in Thai traditional medicine to be effective in *Herpes simplex* infection, *Herpes zoster* and insect bite. An extract from the leaf was found to contain an anti-inflammatory substance effective in animal having inflammation induced by carrageenin (1-3). The anti-inflammatory effect is believed to be due to flavonoids. Studies *in vitro* of the anti-viral activity of *Clinacanthus nutans* against HSV-2 and VZV have been reported (4-5). The leaf extract of *Clinacanthus nutans* was very active in killing HSV-2 and VZV. However the plant had little or no effect on both inhibition of the viruses replication in the infected cells and inhibition of the viruses entering them. These observations imply that the anti-viral effect is a direct interaction and the mechanism of action is thus different from that of acyclovir. Acute and subchronic toxicity tests of *Clinacanthus nutans* revealed

no serious side effects (6). A randomized controlled trial of *Clinacanthus nutans* for the treatment of *Herpes genitalis* was conducted by a group from the Department of Medical Science sponsored by the Government Pharmaceutical Organization (7). Seventy-seven patients, 60 males and 17 females, who had symptomatic *Herpes genitalis* within 48 hours were enrolled. The diagnosis of *Herpes genitalis* was made by clinical features and positive antigen detection or sero-conversion. Twenty percent of the patients were categorized as having primary infection. The patients were allocated at random to groups to receive either 5% *Clinacanthus nutans* extract cream (n = 27) or 5% acyclovir cream (n = 26) or placebo cream (n = 24). Each patient was instructed to apply the cream over the lesions 4 times daily for 6 days. The patients were scheduled for follow-up visits on day 4, 7 and 14 after enrollment. The lesions were crusted within 3 days in 98.6% of the patients in the *Clinacanthus nutans* group compared to 80.8% in the acyclovir group and 12.5% in the placebo group (p < 0.001). The lesions were healed within 7 days in 88.9%, 84.6% and 20.8% of the patients who received *Clinacanthus nutans*, acyclovir and placebo respectively (p < 0.001). The results indicate that *Clinacanthus nutans* is efficacious for the treatment of *Herpes genitalis*, and the efficacy is probably not significantly different from that of acyclovir. A randomized controlled trial of *Clinacanthus nutans* for the treatment of *Herpes zoster* is on going. The preliminary report covers 48 *Herpes zoster* patients aged 15-60 years who had no underlying disease, and had symptoms no longer than 48 hours (8). The patients were allocated at random to receive *Clinacanthus nutans*

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cream or acyclovir cream or placebo cream. The medication was to be applied to the skin lesions 5 times daily for 5 days. The patients receiving *Clinacanthus nutans* had crusting skin lesions within 3 days in 81.3% of cases compared with 27.2% and 0% in the acyclovir group and the placebo group respectively ( $p=0.001$ ). The percentages of healing of the lesions within 7 days were 81.3, 18.2 and 0 for the patients treated with *Clinacanthus nutans*, acyclovir and placebo respectively ( $p < 0.001$ ). The pain scores were also significantly less in the group treated with *Clinacanthus nutans*.

Based on the aforementioned evidence, the Government Pharmaceutical Organization, Ministry of Public Health has made 5% *Clinacanthus nutans* cream available commercially for patients with *Herpes genitalis*. The price of *Clinacanthus nutans* cream is approximately 4 US\$ for 5 grams which while expensive, is still much cheaper than the price of acyclovir. Further studies regarding the use of *Clinacanthus nutans* for the treatment of viral diseases have to be done. They are 1) searching for the active ingredients, 2) improving the attractiveness of the preparation for use because the current preparation is green in color, 3) developing an oral form and an injection form of the drug, 4) performing chronic toxicity

test, 5) testing its anti-viral activity against other viruses. Several of these challenging studies are being undertaken urgently and it is hoped that more useful data will be available in the near future.

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