1. **Network pharmacology to unveil the biological basis of Yishengukang decoction in cancer-induced pain treatment**

**Global Use of Natural Products in Cancer Patient Management**

**Background**: The pathogenesis of cancer-induced pain (CIP) is complex, which involves neuropathic pain characterized by spontaneous pain and increased pain sensitivity.

**Aim:** Previous clinical studies showed Chinese medicine Yishengukang (YG) decoction effectively reduced CIP. However, the commonness in its biological basis remains to be holistically elucidated. Therefore, we tried to find the active ingredients and mechanism by network pharmacology, and to verify that in vivo experiment.

**Method**: Databases and herbs ingredients-disease-target action network were established by network pharmacology, through which the molecular mechanism of diseases and ingredients targets were systematically analyzed. Experimentally, female wistar rats were injected on left tibia with Walker 256 breast cancer cells to establish CIP model and treated with YG and pathway inhibitor as the intervention groups.

**Results**: A visual and integrated disease and function network of herbs compounds targets pathway was constructed and analyzed. It showed that 50 components of YG modulated 89 targets of neuropathic pain. Through in-depth network analysis, it demonstrated that the mechanism of YG in cancer pain treatment was p38MAPK pathway with 13 herb ingredients showing strong relationship. In the vivo study, we demonstrated that YG could reduce the pain behaviors by regulating the phosphorylation level of p38 in brain hippocampus and spinal regions and the expression of inflammatory pain factors, while the pain and activation of **microglia decreased in rats after the application of p38 MAPK inhibitor.**

**Conclusions**: The present study showed that YG decoction played a role in regulating central sensitization of cancer pain. It provided a systematic perspective on the relationship between herbs and disease processes and revealed the possible pharmacological effects of various components in herbal products, which promoted symptom-based drug discovery and therapy.

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