Could *Scutellaria barbata* D. Don be used for treating lung cancer and SARS-CoV-2?

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Dear Editor,

Scutellaria barbata D. Don (SBD) is a perennial herb and belongs to the "*Lamiaceae*" family. This is widely used in China for a long time as Traditional Chinese Medicine (TCM). Based on the TCM theory, SBD is in the category of "Heat-Clearing". Its functions are to remove heat and detoxification, disperse blood stasis and diuresis.[1] Lung cancer is a leading cause of death worldwide and has an estimated 2.09 million deaths in 2018 according to the World Health Organization (WHO).[2]

Growing evidence has shown that the SBD possessed anti-inflammatory and anti-cancer properties. The functional components in SBD including phenolics, flavonoids, chlorophylls, carotenoids, carotenoids, and chlorophylls which inhibited the production of lipopolysaccharide-induced nitric oxide, prostaglandin E_2, interleukin-6, and interleukin-1β, as well as the expressions of phosphor extracellular signal-regulated kinase and phosphor-c-Jun N-terminal kinase (p-JNK) on RAW 264.7 cells.[3] Yin *et al.* reported the ethanol extracts of SBD inhibited the growth of A549 human lung cancer cell line. Its mechanism involved cell apoptosis such as DNA damage, cell cycle control, nucleic acid binding, and protein phosphorylation. The cytotoxic effects of SBD on A549 cells with IC_{50} of 0.21 mg/mL.[4] Chen *et al.* found that the SBD in lung cancer was related to the P38/SIRT1-regulating cell apoptosis through G2/M phase arrest and ER stress, intrinsic mitochondrial, and extrinsic FAS/FASL-mediated pathways. SBD reduced the lung tumor size with decreased proliferation and angiogenesis, as well as increased apoptosis of lung cancer cells.[5] Gong *et al.* also indicated the SBD inhibited the lung tumor growth of Lewis-bearing C57BL/6 mice through modulating the immune function which provided the possible application of immunotherapy for the treatment of Non-Small-Cell Lung Cancer (NSCLC) in an early and advanced stage to further human clinical study.[6]

SBD is TCM and its formulation revealed good cytotoxicity on lung cancer. The TCM formulation include 0.5-1.5g SBD, 0.5-1.5g *Prunellae spica*, 0.5-1.5g *Antrodia camphorata*, 0.5-1.5g *Curcumae rhizome*, 0.5-1.5g *Paeoniae suffruticosae cortex*, 0.5-1.5g *Patriniae herba*, 0.5-1.5g *Ixeris herba*, and 0.5-1.5g *Phellinus linteus*. Tsai *et al.* indicated that this TCM formulation inhibited lung cancer. Treatment dosage was typically 4 to 300 g per day for the average human.[7] Another research from Wang focused on a TCM prescription named Lian-Jia-San-Jie-Fang (LJSJF), which synergistically regulated the Epidermal Growth Factor Receptor (EGFR) or p53 signaling pathways. It downregulated in EGFR and downstream signaling targeted mTOR and p38 MAPK to suppress the growth of lung cancer.[8]

Coronavirus disease 2019 (COVID-19) is caused by SARS-CoV-2 infection, which has been spread rapidly across the world. It is mediated by the recognition of a Receptor-Binding Domain (RBD) between the S protein and Angiotensin-Converting Enzyme 2 (ACE2) receptor on the host cell surface, and the activation of S protein bind to TMPRSS2 transmembrane serine protease 2 that is an inhibitor to prevent the virus invasion.[9] In early 2021, Huang *et al.* reported SBD may effectively prevent SARS-CoV-2 infection and replication through inhibiting M^{pro} and TMPRSS2 protease activities.[10]

The above information demonstrates that *Scutellaria barbata* D. Don is a possible candidate in Chinese medicine for treating lung cancer and SARS-CoV-2 as it possesses anti-inflammatory, anti-cancer, and anti-viral properties. According to the TCM theory, SBD functions are to remove heat and detoxification within the body. Its TCM formulation and prescription are effective to inhibit lung cancer and enhance the immune system. However, much more works need to be done, especially for the multiple TCM formulation on the safety assessment of human clinical trials. SBD combined with the usage of other Chinese medicine may be a good

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choice to increase its functions or properties to treat various cancers and respiratory diseases.

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