ORAL DISEASES

Oral Diseases (2011) 17, 7–12. doi:10.1111/j.1601-0825.2010.01706.x

www.wiley.com

INVITED MEDICAL REVIEW

Traditional Chinese medicine and oral diseases: today and tomorrow

LW Zheng[1], H Hua[2], LK Cheung[1]

[1]*Oral & Maxillofacial Surgery, Faculty of Dentistry, The University of Hong Kong;* [2]*Department of Oral Medicine and Traditional Chinese Medicine, Peking University, School and Hospital of Stomatology, Beijing, China*

With a history of over 2000 years, traditional Chinese medicine (TCM) evolves into a unique system of diagnosing and treating illnesses. It is a challenge to convey the fundamentals of this traditional medicine to our Western colleagues because of the differences in language, philosophy and concept of diagnosis and treatment. This review attempts to tackle these barriers by introducing several widely used Chinese medicines for treating oral diseases. China Journals Full-text Database and Pubmed were used as the searching engines. Although many studies have demonstrated that the Chinese medicines are effective in treating oral diseases including recurrent aphthous stomatitis, oral lichen planus, leukoplakia, and Sjögren's syndrome, most of them lacked standard criteria of post-treatment assessment and laboratory evidence. Randomized controlled clinical trials with specific assessment criteria are required to close the gap between TCM and evidenced-based medicine.

Oral Diseases (2011) **17**, 7–12

Keywords: Chinese medicine; oral disease; treatment; herbology

Introduction

With a history of more than 2000 years, Traditional Chinese Medicine (TCM) has formed a unique system to diagnose and treat a variety of diseases. The therapeutic approaches in typical TCM include herbal therapy, acupuncture, dietary therapy, and qigong exercises. Herbology is one of the most important treatment modalities utilized in TCM. Each herbal medicine prescription is a cocktail of several herbs. The Chinese pharmacopoeia lists over 6000 medicinal substances and their properties. Among these substances around 600 herbs are commonly used today (Unschuld, 1986, Fratkin and Dharmananda, 2001).

Chinese patent medicine (zhōng chéng yào) referes to the drugs made according to a standardized formula (even though the word "patent" is used none of the manufactures have exclusive rights over these formulae). Several herbs and other ingredients are dried, ground and mixed according to the formulae. These drugs are available in pharmacies as condensed pills, oral liquids, granules or capsules. Thus all Chinese patent medicines with the same name are expected to have the same proportions of ingredients. Most Chinese medicines with natural ingredients can be taken as a long-term treatment with fewer side effects. Chinese medicines are not indicated for the treatment of acute illness but are best suited for managing non-severe chronic diseases.

Although TCM has been used for treating oral diseases for a very long time, it is barely known and understood by clinicians and scientists outside China. It is a challenge to make this traditional medicine understood by our Western colleagues because of the huge differences in language, philosophy and concept of diagnosis and treatment. This review attempts to tackle this difficulty by introducing five Chinese medicines widely used in the treatment of some common oral diseases, such as recurrent aphthous stomatitis (RAS), oral lichen planus (OLP), leukoplakia and Sjögren's syndrome (SS) (Table 1). Totally 128 clinical reports were retrieved from the China Journals Full-text Database and Pubmed. However, most of the articles were case reports or case series without standard criteria for evaluating the effectiveness of treatment. Therefore only reports using the standard criteria issued by Society of Oral Mucosal Disease of Chinese Stomatological Association (2001, 2005) were selected.

Liuwei Dihuang (liù wèi dì huáng)

Liuwei Dihuang is consists of six ingredients extracted from natural herbs including: radix rehmanniae, fructus

Correspondence: Prof. Lim Kwong Cheung, Oral & Maxillofacial Surgery, The Prince Philip Dental Hospital, 34 Hospital Road, Hong Kong SAR, China. Tel: 852 28590262, Fax: 852 28575570, E-mail: lkcheung@hku.hk; Prof. H. Hua, Department of Oral Medicine and Traditional Chinese Medicine, Peking University, School and Hospital of Stomatology, 22 Zhongguancun Nandajie, Beijing, 100081, China. Tel: 86-10-62179977 ext 5349, Fax: 86-10-62173402, E-mail: honghua1968@yahoo.com.cn
Received 30 March 2010; revised 1 April 2010, accepted 1 April 2010

Table 1 Application of Chinese medicines in oral diseases

Chinese medicine	*Oral mucosal diseases*
Liuwei Dihuang	Recurrent aphthous stomatitis Sjögren's syndrome Oral lichen planus
Tripterygium glycosides	Recurrent aphthous stomatitis Oral lichen planus Sjögren's syndrome
Stomatitis-healing granule	Recurrent aphthous stomatitis
Composite Taixian tablet	Oral lichen planus
Zengshenping	Oral lichen planus Oral leukoplakia

corni officinalis, radix dioscoreae oppositae, alismatis rhizoma, sclerotium poriae cocos and cortex moutan radicis. It is one of the most commonly used Chinese medicines in the treatment of various local and systemic chronic diseases.

Several reports demonstrated that long-term administration of LiuWei DiHuang could modulate the cell-mediated immune response of RAS patients by correcting the imbalance of T-lymphocyte subsets (Zou and Zhang, 2003, Sun, 2004). Following the investigation of 30 RAS patients and 30 healthy volunteers, Sun (2004) reported that the RAS patients had depressed $CD3^+$, $CD4^+$ cell counts and elevated $CD8^+$ cell counts. The $CD4^+/CD8^+$ ratio was also depressed. Six months after oral administration of Liuwei Dihuang, the $CD3^+$, $CD4^+$ cell counts and $CD4^+/CD8^+$ ratio became elevated significantly. All these values were not statistically different from the healthy volunteers. Clinical studies in different centers showed a varied response of the RAS patients to Liuwei Dihuang: 13.3–70.0% healed, 10.0–76.9% improved, and 3.3–20.0% patients had no positive response to this medication (Table 2) (Zhou, 1995, Lǔ, 2001, Sun, 2003, Xie, 2004, Jia and Luo, 2006, Tong and Feng, 2008, Wang, 2009).

Shen (2002) used Liuwei Dihuang to treat 30 SS patients. Three months after the treatment, Schimer test, tear break-up time test, rose-bengal score dye test and salivary flow test demonstrated a reduction of dryness of the mouth and eyes in all the patients. The rheumatoid factor became negative in 10/16 (62.5%) patients. Six months after the treatment, antinuclear antibodies of 10/23 (43.5%) patients and anti-SSA/anti-SSB antibodies of 13/28 (46.4%) patients became negative. Zhao (2006) reported the outcome of a long-term administration (1–3 years) of Liuwei Dihuang for patients with SS. At the 6-month follow-up after stopping the mediation, two patients (6.7%) had complete remission and 15 patients (50%) had reduced dryness without recurrence. Nine patients (30%) had alleviated symptoms while taking the medication but recurred after stopping it. Four patients (13.3%) did not respond to the treatment.

Xuan (1997) investigated the combined administration of Liuwei Dihuang and retinoic acid cream in treatment of 43 patients with OLP. They found that the combined medications were more effective than retinoic acid cream alone, particularly for treating the patients with a history of OLP less than 3 years.

Tripterygium glycosides (léi gōng téng duō dài)

Tripterygium wilfordii is a native plant that grows in many parts of China and Burma. It has been commonly used in the treatment of a wide spectrum of autoimmune and inflammatory diseases (Tao *et al,* 2001, 2002, Qiu and Kao, 2003, Kumar *et al,* 2005, Canter *et al* 2006). Studies have demonstrated that *T. wilfordii* was capable of reducing the serum levels of IgG and correcting the imbalanced T-lymphocyte subsets (Li *et al,* 1996, Wong *et al,* 1998, Fang *et al,* 2006). A recent study also showed that *T. wilfordii* inhibited tumor progression by its anti-angiogenic activity (He *et al,* 2009). However, it is notable that *T. wilfordii* is the most toxic among all the Chinese herbs. Its adverse effects mainly include gastrointestinal disturbance, infertility and suppression of immune system (Wang, 1993). Tripterygium glycosides are extracted from the peeled roots of *T. wilfordi*. This is effective at a much lower dosage and has less adverse effects compared to other preparations of *T. wilfordii*.

Li *et al* (1996) treated 27 RAS patients with oral Tripterygium glycosides for 3 months. The plasma soluble interleukin-2 receptor levels reduced from 601.5 ± 225.2 U ml^{-1} to 380.8 ± 94.2 U ml^{-1} which was not significantly different from the healthy volunteers (302.0 ± 105.3 U ml^{-1}). Studies also reported that

Table 2 Effect of Liuwei Dihuang for treating RAS

	Number of cases	*Prognosis*			
		Heal (%)	*Marked improvement*	*Moderate improvement*	*No improvement (%)*
Lǔ, 2001	30	13.3	36.7%	43.3%	6.7
Xie, 2004	50	18.0	38.0%	34.0%	10.0
Sun, 2003	40	25.0	50.0%	17.5%	7.5
Tong, 2008	30	70.0	10.0%	20.0	
Zhou, 1995	52	19.2	76.9%	3.9	
Wang, 2009	80	55.0	32.5%	12.5	
Jia, 2006	120	52.5	26.7%	17.5%	3.3

Heal: complete remission of the pain and lesions, no recurrence within 1 year; Marked improvement: complete remission of the pain and lesions, no recurrence within 6 months; Moderate improvement: reduction of pain, size and number of lesions, interval of recurrence is prolonged; No improvement: no reduction/worsening in the pain, size and number of lesions (Society of Oral Mucosal Disease of Chinese Stomatological Association 2001).

Tripterygium glycosides reduced the serum nitric oxide of RAS patients to normal levels (Bu *et al,* 2006, Ma *et al,* 2006). Zhang (2003) compared the effectiveness of Tripterygium glycosides and hydrocortisone for treating RAS patients. Thirty patients received oral hydrocortisone (started at 60 mg day^{-1} and gradually reduced to 10 mg day^{-1} for 10 days), and 30 patients were treated with oral Tripterygium glycosides (60 mg day^{-1} for 10 days). Results showed that Tripterygium glycosides was as effective as hydrocortisone.

Many studies have demonstrated the effectiveness of Tripterygium glycosides in the treatment of OLP patients (Table 3). In all these reports, an overall 20.0–84.0% of the patients markedly improved, 12.0–45.8% moderately improved, and 4.0–50.0% had no improvement after treatment (Zheng, 1988, Yin *et al,* 1996, Jiang and Wang, 2000, Xu, 2001, Han *et al,* 2007). Zheng (1988) investigated 100 OLP patients, 66 without erosive lesions and 34 with erosive lesions. All patients with reticular OLP showed improvement after 1 month treatment with Tripterygium glycosides, while plaque-like lesion required longer treatment and improvement was found after 2–3 months. However, effectiveness of Tripterygium glycosides for treating erosive lesions was less. Tripterygium glycosides also demonstrated promising results in the treatment of OLP while being used in combination with other therapies such as Nd-YAG laser, triamcinolone and chloroquine (Yin *et al,* 1996, Guan and Zhu, 2003, Zhang *et al,* 2008).

Huang and Chen (1996) reported a clinical trial where *T. wilfordii* were used to treat 18 patients with SS. Three months after treatment, 16 patients showed increased salivary and tear flow and reduced symptoms of dry mouth and dry eye. The increased erythrocyte sedimentation rate in 7/11 (63.6%) and IgG in 10/13 (76.9%) patients returned to normal levels. The circulatory immune complex in 12/15 (80%) and antinuclear antibody in 7/11 (63.6%) patients became negative.

Stomatitis-healing granule (kǒu yán qīng chōng jì)

Stomatitis-healing granule is made of cochinchinese asparagus root, tuber ophiopogonis japonici, radix scrophulariae ningpoensis, flos Lonicerae japonicae and radix glycyrrhizae uralensis. An animal study using a mice model showed that Stomatitis-healing granule reduced the permeability of capillaries, inhibited delayed-type hypersensitivity and decelerated granuloma growth. *In vitro* assessment demonstrated inhibition of *Staphylococcus aureus*, *Streptococcus pneumoniae* and hemolytic streptococcus A and B (Li *et al,* 1999). Clinically Stomatitis-healing granule is mainly used for treating RAS. In all these studies an overall 0–60% patients healed, 17.1–62.5% improved markedly, 11.6–44.8% improved moderately after treatment. 3.1–12.1% patients had no positive response to this medication (Table 4) (Zhen *et al,* 2002, Wang and Wang, 2004, Meng, 2006a, 2006b, Huang, 2007).

Table 3 Effect of Tripterygium glycosides for treating OLP

		Prognosis (%)		
	Number of cases	*Marked improvement*	*Moderate improvement*	*No improvement*
Zheng, 1998	100	84.0	12.0	4.0
Yin, 1996	30	23.3	30.0	46.7
Xu, 2001	30	20.0	30.0	50.0
Jiang, 2000	24	41.7	45.8	12.5
Han, 2007	30	66.7	13.3	20.0

Marked improvement: complete remission of erosion and pain, no/-mild white streak; Moderate improvement: reduction of pain, white streak, and size of erosion; No improvement: no reduction/worsening of pain, white streak, and size of erosion (Society of Oral Mucosal Disease of Chinese Stomatological Association 2005).

Table 4 Effect of Stomatitis-healing granule for treating RAS

		Prognosis (%)			
	Number of cases	*Heal*	*Marked improvement*	*Moderate improvement*	*No improvement*
Meng, 2006b	32	56.3	28.1	12.5	3.1
Huang, 2007	70	60.0	17.1	14.3	8.6
Wang, 2004	32	0	62.5	34.4	3.1
Huang, 2007	70	60.0	17.1	14.3	8.6
Meng, 2006a	116	19.2	23.9	44.8	12.1
Zhen, 2002	86	48.8	29.1	11.6	10.5

Composite Taixian tablet (fù fāng tái xiǎn piàn)

Composite Taixian tablet contains radix ligustici chuanxiong, radix ginseng, radix paeoniae lactiflorae, semen persicae and radix et caulis jixueteng. It is mainly used for the treatment of OLP. An *in vitro* study showed that Composite Taixian tablet reduced the platelet adhesion of OLP patients without affecting platelet aggregation, which suggested its ability for improving blood viscosity and microcirculation (Lin and Zhou, 1992, Lin *et al,* 1992).

Studies demonstrated that after being treated with Composite Taixian tablet, the overall rates of marked improvement were 23.3–36.9%, moderate improvement were 35–46.7%. Around 16.4–41.7% patients had no positive response (Table 5) (Zeng *et al,* 1993, Pan and Yi, 1997, Zhang *et al,* 2001). A clinical trial by Pan and Yi (1997) recruited 30 patients (26 with non-erosive and 4 with erosive OLP). The 26 patients with non-erosive OLP were randomly assigned to an experimental group (composite Taixian tablet) and a control group (placebo). The four patients with erosive OLP were evenly

Table 5 Effect of Composite Taixian tablet for treating OLP

		Prognosis (%)		
	Number of cases	*Marked improvement*	*Moderate Improvement*	*No improvement*
Pan, 1997	15	36.9	46.7	16.4
Zeng, 1993	139	26.6	54.7	18.7
Zhang, 2001	60	23.3	35.0	41.7

assigned to the experimental and control groups. After 3 months of treatment, six patients in the experiment group improved markedly (40%), seven patients improved moderately (47%) and two patients did not response to the medication (13%). In the control group, none of the patients showed marked improvement, five patients improved moderately (33%) and 10 patients did not improve (67%). However, the study did not specifically state the prognosis of the four patients with erosive lesions.

Zengshengping (zēng shēng píng)

Zengshengping is composed of vietnamese sophora root, bistort rhizome, north valerianaceae, cortex dictamni, *Prunella vulgaris* L and *Dioscorea bulbifera*. Zengshengping is known to modulate immune reactions, inhibit production of inflammatory cytokines, suppress tumor cell proliferation and reduce the incidence of squamous cell carcinoma (Cai *et al,* 1980, Lin, 1990, Fan, 1993, Wang *et al,* 1994).

Zengshengping has been used to treat patients with precancerous lesions of the esophagus successfully since 1980s. Lin *et al* (1998) reported after giving Zengshengping for 3 years, the cancer incidence reduced from 5.3% (102/1922) to 2.79% (28/1054). Hou and colleagues (2002) reported that after 3 years blocking treatment of esophageal epithelia dysplasia with the same medication, cancer incidence reduced from 3.85% (102/2649) to 2.01% (28/1396). A randomized controlled clinical trial by Sun *et al* (2010) showed that Zengshengping significantly reduced the size of the oral lesion in 67.8% (40/59) patients with leukoplakia, which was significantly higher than that in the control group (17% (9/53)) using placebo. The chemopreventive effect of Zengshengping was significantly associated with the decrease of two cell proliferation biomarkers, silver stained nucleoli organizer region and proliferating cell nuclear antigen-labeling index. Shang *et al* (2004) reported that after treatment with Zengshengping, the size of oral leukoplakia reduced significantly in 74.6% (47/63) patients. Zengshengping has been also used for treating OLP, with a 79.4% (50/63) (Sun *et al,* 2004) and 90% (90/100) (Cao *et al,* 2001) patients positively responding to this medication.

Conclusion

Although TCM has been used for over 2000 years in the treatment of various diseases, it is not fully understood and accepted by the clinicians outside China. Even in China, not all the practitioners believe its effectiveness. The major barrier between the TCM and contemporary medicine is not only the language, but the basic concepts in diagnosis and management of the disease. While the contemporary medicine developed from an evidence-based system, the TCM is basically experience-based. It was a challenge to search and select high quality reports from hundreds of papers related to this topic. Most of the clinical studies were case reports or case series without good controls. Standard criteria for post-treatment assessment and laboratory evidence supporting the findings and conclusions were lacking in most of the reports. Many Chinese clinicians and scientists have been making a great effort to build the missing link between the 1000-year-experience based knowledge and the evidence-based medical sciences. Even though the authors planed a systematic review at the beginning, we were compelled to perform a general review giving a glimpse of TCM in oral diseases because of the lack of high quality animal and clinical studies. The effective chemical components, optimal ratios of the herb ''cocktail'' and the mechanisms of the medicines on different diseases need to be explored by high quality laboratory and animal experiments, as well as randomized controlled clinical trials.

Acknowledgements

We gratefully acknowledge Dr. Ma L and Dr. Jayaratne YS of The University of Hong Kong for their great effort in literature searching and technical assistance.

Author contributions

All authors contribute to this manuscript.

References

Bu G, Ma WB, Qi L (2006). Change of serum nitric oxide and nitric oxide synthase in recurrent aphthous stomatitis patients treated with tripterygium glycosides. *Jian Yan Yi Xue* **21:** 146–147.

Cai HY, Shu YJ, Wang GQ, *et al*. (1980). Therapy of severe epithelial dysplasia of esophagus using Zengshengping. *Zhonghua Zhong Liu Za Zhi* **2:** 92–95.

Canter PH, Lee HS, Ernst E (2006). A systematic review of randomised clinical trials of *Tripterygium wilfordii* for rheumatoid arthritis. *Phytomedicine* **13:** 371–377.

Cao J, Zhou RJ, Deng HP (2001). Effect of Zengshengping for treating oral lichen planus: a clinical study. *Shi Yong Kou Qiang Yi Xue Za Zhi* **17:** 50–51.

Fan X (1993). Inhibitory effect of Zengshengping and retinamide on precancerous lesions of the bladder in rats. *Zhongguo Yi Xue Ke Xue Yuan Xue Bao* **15:** 71–73.

Fang X, Li JY, Ou YH, Gan J (2006). *Tripterygium wilfordii* slow-releasing film for treating recurrent aphthous stomatitis. *Jiangxi Yi Xue Yuan Xue Bao* **46:** 154–155.

Fratkin J, Dharmananda S (2001). *Chinese herbal patent medicines: the clinical desk reference*. Shya Publications: Boulder, Colo.

Guan ZJ, Zhu XH (2003). Combined administration of chloroquine and tripterygium glycosides in treatment of oral lichen planus. *Xian Dai Kou Qiang Yi Xue Za Zhi* **17:** 132.

Han XH, Nan XL, Wu YT (2007). Application of total glucosides of paeony caosules and tripterygium glycosides for treating oral lichen planus. *Yao Wu Yu Lin Chuang* **4:** 74–75.

He MF, Liu L, Ge W, *et al*. (2009). Antiangiogenic activity of *Tripterygium wilfordii* and its terpenoids. *J Ethnopharmacol* **121:** 61–68.

Hou J, Lin PZ, Chen ZF, *et al*. (2002). Field population-based blocking treatment of esophageal epithelia dysplasia. *World J Gastroenterol* **8:** 418–422.

Huang HF, Chen L (1996). *Tripterygium wilfordii* in the treatment of Sjögren's syndrome: report of 18 cases. *Kou Qiang Yi Xue* **16:** 139–210.

Huang MH (2007). Effect of stomatitis-healing granule for treating recurrent aphthous stomatitis: report of 70 cases. *Zhongguo Zhong Xi Yi Jie He Xiao Hua Za Zhi* **15:** 403–404.

Jia YJ, Luo YX (2006). Clinical assessment of 120 recurrent aphthous stomatitis patients treated with Liuwei Dihuang. *Shanxi Zhong Yi* **27:** 432–433.

Jiang S, Wang GY (2000). Application of Tripterygium glycosides for treating oral lichen planus: report of 24 cases. *Wei Fang Yi Xue Yuan Xue Bao* **22:** 308.

Kumar DS, Lau CS, Wan JM, Yang D, Hyde KD (2005). Immunomodulatory compounds from *Pestalotiopsis leucothes*, an endophytic fungus from *Tripterygium wilfordii*. *Life Sci* **78:** 147–156.

Li HR, Yu WY, Zheng J (1996). Influence of *Tripterygium glycosideson* on plasma soluble interleukin-2 receptor in patients with recurrent aphthous stomatitis. *Zhongguo Zhong Xi Yi Jie He Za Zhi* **16:** 365.

Li ZS, Zhang XN, Liang Y, *et al*. (1999). Pharmacodynamics anslysis of stomatitis-healing granule. *Zhong Yao Xin Yao Yu Lin Chuang Yao Li* **10:** 216–218.

Lin M, Zhang WQ, Zhou M (1992). Effect of composite taixian tablet on platelet function of patient with lichen planus: an *in vitro* study. *Shi Yong Kou Qiang Yi Xue Za Zhi* **8:** 134–136.

Lin M, Zhou M (1992). Effect of composite taixian tablet on platelet electrophoresis time of patient with lichen planus. *Kou Qiang Yi Xue Zong Heng* **11:** 214–215.

Lin P (1990). Inhibitory effect of Zengshengping, retinamide and riboflavin on precancerous lesions of the esophagus. *Zhongguo Yi Xue Ke Xue Yuan Xue Bao* **12:** 235–245.

Lin P, Chen Z, Hou J, Liu T, Wang J (1998). Chemoprevention of esophageal cancer. *Zhongguo Yi Xue Ke Xue Yuan Xue Bao* **20:** 413–418.

Lǔ Y (2001). Application of Liuwei Dihuang for treating recurrent aphthous stomatitis: report of 30 cases. *Guangxi Zhong Yi Xue Yuan Xue Bao* **18:** 36–7.

Ma WB, Bu G, Xie WZ, Li CX (2006). Change of serum nitric oxide and nitric oxide synthase in recurrent aphthous stomatitis patients treated with Tripterygium glycosides. *Shi Yong Kou Qiang Yi Xue Za Zhi* **22:** 267–268.

Meng FK (2006a). Clinical study of stomatitis-healing granules for treatment of 116 patients with recurrent aphthous stomatitis. *Zhong Hua Yi Xue Shi Jian Za Zhi* **5:** 71.

Meng SY (2006b). Clinical assessment of Stomatitis-healing granule for treating recurrent aphthous stomatitis. *Yi Yao Lun Tan Za Zhi* **27:** 71.

Pan XY, Yi L (1997). Effectiveness assessment of Composite Taixian tablet for treating oral lichen planus. *Lu Zhou Yi Xue Yuan Xue Bao* **20:** 373–374.

Qiu D, Kao PN (2003). Immunosuppressive and anti-inflammatory mechanisms of triptolide, the principal active diterpenoid from the Chinese medicinal herb *Tripterygium wilfordii* Hook. f. *Drugs R D* **4:** 1–18.

Shang JL, Han B, Shi AM (2004). Clinical assessment of using Zengshengping for treating oral leukoplakia. *Zhongguo Zhong Yi Yao Xin Xi Za Zhi* **11:** 527–528.

Shen K (2002). Application of Liuwei Dihuang for treatment of primary Sjögren's syndrome: report of 30 cases. *Shandong Zhong Yi Za Zhi* **21:** 467–469.

Society of Oral Mucosal Disease of Chinese Stomatological Association (2001). Standard for evaluation of effect for recurrent aphthous stomatitis. *Lin Chuang Kou Qiang Yi Xue Za Zhi* **17:** 209.

Society of Oral Mucosal Disease of Chinese Stomatological Association (2005). Standard for evaluation of effect for oral lichen planus. *Zhongguo Kou Qiang Yi Xue Za Zhi* **40:** 112.

Sun LL (2003). Clinical study of Liuwei Dihuang for treating recurrent aphthous stomatitis. *Zhongguo Wu Zhen Xue Za Zhi* **3:** 1344–1345.

Sun LL (2004). Influence of Liuwei Dihuang on cell-mediated immuno-reaction of recurrent aphthous stomatitis patients. *Shi Yong Kou Qiang Yi Xue Za Zhi* **20:** 647–648.

Sun Z, Guan X, Li N, Liu X, Chen X (2010). Chemoprevention of oral cancer in animal models, and effect on leukoplakias in human patients with ZengShengPing, a mixture of medicinal herbs. *Oral Oncol* **46:** 105–110.

Sun Z, Shen SL, Guan XB, Wang R (2004). Application of Zengshengping for treating oral lichen planus. *Beijing Kou Qiang Yi Xue* **12:** 212–213.

Tao X, Cush JJ, Garret M, Lipsky PE (2001). A phase I study of ethyl acetate extract of the Chinese antirheumatic herb *Tripterygium wilfordii* hook F in rheumatoid arthritis. *J Rheumatol* **28:** 2160–2167.

Tao X, Younger J, Fan FZ, Wang B, Lipsky PE (2002). Benefit of an extract of *Tripterygium wilfordii* Hook F in patients with rheumatoid arthritis: a double-blind, placebo-controlled study. *Arthritis Rheum* **46:** 1735–1743.

Tong LP, Feng J (2008). Liuwei Dihuang for treating recurrent aphthous stomatitis. *Lin Chuang Yi Xue* **28:** 87–88.

Unschuld PU (1986). *Medicine in China: a history of pharmaceutics*. University of California Press: Berkeley.

Wang CD (1993). Active ingredients, pharmacological action and clinical application of *Tripterygium wilfordii*. *Zhongguo Zhong Xi Yi Jie He Za Zhi* **13:** 507–509.

Wang DC, Wang DB, Zhang JS (1994). Experimental study on pharmacologic effects of Zengshengping. *Zhonghua Zhong Liu Za Zhi* **16:** 419–423.

Wang LY, Wang WM (2004). Clinical study of using stomatitis-healing granule for treating recurrent aphthous stomatitis: report of 34 cases. *Jiangsu Zhong Yi Yao* **25:** 39–40.

Wang Y (2009). Study of using Liuwei Dihuang for treatment of recurrent aphthous stomatitis. *Zhong Xi Yi Jie He Xi Nao Xue Guan Zi Zhi (Chinese Journal of Integrative Medicine on Cardio-/ Cerebrovascular Disease)* **7:** 880–881.

Wong ZQ, Su H, Xu JB (1998). Influence of Tripterygium glycosides on modulating immuno-reaction of patients with recurrent aphthous stomatitis. *Xian Dai Lin Chuang Yi Xue Sheng Wu Gong Cheng Xue Za Zhi* **4:** 92–93.

Xie X (2004). Effectiveness of Liuwei Dihuang for treating recurrent aphthous stomatitis. *Beijing Kou Qiang Yi Xue* **12:** 102.

Xu JY (2001). Application of Tripterygium glycosides for treating oral lichen planus: a primary report. *Lin Chuang Yan Jiu* **10:** 2243–2244.

Xuan JP (1997). Clinical study of Liuwei Dihuang in treatment of oral lichen planus: report of 43 cases. *Zhejiang Zhong Yi Xue Yuan Xue Bao* **21:** 34.

Yin C, Liang M, Wang X (1996). Effect of triamcinolone and Tripterygium glycosides in treatment of 110 patients with lichen planus. *Guangdong Ya Ping Fang Zhi* **4:** 18–19.

Zeng GM, Li BQ, Wang XY, *et al*. (1993). Clinical study of Composite Taixian tablet for treating oral lichen planus. *Hua Xi Kou Qiang Yi Xue Za Zhi* **11:** 45–47.

Zhang HL (2003). Using of Tripterygium glycosides for treating recurrent aphthous stomatitis. *Kou Qiang Yi Xue* **23:** 35–36.

Zhang P, Xu SS, Zhang Q, Zhang YD (2001). Clinical assessment of Composite Taixian tablet in treatment of oral lichen planus. *Lin Chuang Kou Qiang Yi Xue Za Zhi* **17:** 209.

Zhang T, Xu ZP, Jiao HM (2008). Combined therapy of Tripterygium glycosides and Nd-YAG laser for treating oral lichen planus. *Xi Bei Yao Xue Za Zhi* **23:** 316–317.

Zhao DS (2006). Liuwen Dihuang for treating Sjögren's syndrome: a clinical assessment. *Guang Ming Zhong Yi* **21:** 50–51.

Zhen YC, Huang YH, Lin F, Huang QZ (2002). Stomatitis-healing granule and Aloe gel for treating recurrent aphthous stomatitis: report of 86 cases. *Hubei Zhong Yi Za Zhi* **24:** 31–32.

Zheng JL (1988). Tripterygium glycosides for treating oral lichen planus: report of 100 cases. *Lin Chuang Kou Qiang Yi Xue Za Zhi* **4:** 126–127.

Zhou WB (1995). Clinical assessment of Liuwei Dihuang in treatment of 52 patients with recurrent aphthous stomatitis. *Shi Yong Zhong Yi Yao Za Zhi* **3:** 41.

Zou J, Zhang J (2003). *Pharmacology and application of Chinese patent medicine*. Fu dan da xue chu ban she: Shanghai.