

# A Literature Review of Chinese Herbal Medicine in the Treatment of Gastritis



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Gastritis is defined as “inflammation of the gastric mucosa” (Beers and Berkow, 2004, p245) with formal diagnosis made histologically. Over 80% of cases are caused by the non-sporing curvilinear gram-negative bacteria *Helicobacter pylori* (Liu and Crawford, 2005) with the rest being autoimmune, infection by other microbes, duodenogastric reflux and other specific causes (Clark and Silk, 2002). It may lead to erosion of the stomach lining at which point it is referred to as atrophic or erosive gastritis. Acute and chronic forms can also be differentiated with chronic cases able to remain asymptomatic throughout life unless they progress to complication. When symptoms do present they are usually due to erosion and cause a gnawing or burning stomach pain, nausea, vomiting and a feeling of fullness after eating. In severe cases there may be bleeding if the gastric mucosa is perforated or there may be a progression into gastric cancer. This often presents as the vomiting of “coffee grounds” rather than fresh blood but both situations require immediate referral for investigation.

Other diseases with similar presentations such as functional dyspepsia or peptic ulcer are also often included under the term “gastritis” in casual literature (NHS Choices, 2014). Functional dyspepsia has no organic cause although it is often treated in the same way despite inconsistent results (Du et al., 2016). Emotional causes, once considered the main aetiology of gastritis, remain controversial but do not cause inflammation without another agent present (Clark and Silk, 2002). Peptic ulcers may be a complication of gastritis but are also possible without infection especially from the use of Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) and alcohol which may erode the endothelium without inflammation and even reduce the rates of *H. pylori* infection (Kuepper-Nybelen, Rothenbacher and

Brenner, 2005). This is becoming more common in the developed world where antibiotic therapies have dramatically reduced the *H. pylori* carrying population but the use of painkillers rises.

## Western Medicine

The discovery of *H. pylori* by Marshall and Warren (1984) and subsequent dramatic self-infection by one of the researchers (Marshall et al., 1985) proved the role of bacteria in gastritis. This caused a revolutionary paradigm shift away from the prevailing opinion that the stomach was too acidic to support life. It is now known that the stomach is host to a variety of bacteria whose profile is altered in various disease states although to what extent *H. pylori* colonisation perturbs the healthy ecology or how the existing microbiota affect the outcome of an *H. pylori* infection is currently unclear (Nardone and Compare, 2015). This has also enabled simple breath tests for the detection of *H. pylori* colonisation by ingesting  $^{13}\text{C}$  Urea which is broken down by *H. pylori* to produce  $^{13}\text{CO}_2$  in the breath detectable by mass spectrometry although blood, stool and endoscopic examinations are also available (Clark and Silk, 2002).

## Aetiology and Pathology:

The mechanisms that *H. pylori* uses have been well documented (Sheh and Fox, 2013). Upon infection *H. pylori* utilises the enzymes urease and  $\alpha$ -carbonic anhydrase to raise the pH of the local area until it can establish itself in the inner mucus layer and attach to epithelial cells. The host then mounts an acute inflammatory response which *H. pylori* defends against using further enzymes which detoxify and inhibit the

attacks from the host leading to a chronic inflammatory state mediated mainly by T-cell lymphocytes from the hosts adaptive immune system. Over time this can progress through a series of discrete steps known as the Correa pathway to atrophy, metaplasia, dysplasia and adenocarcinoma. As the specialised acid secreting parietal cells are lost the pH of the stomach rises allowing *H. pylori* to colonise other areas of the stomach along with other bacteria not normally able to survive in such an acidic environment. These changes in microbiota are associated with gastric cancer although which ones are causative is not clear and *H. pylori* is noticeably absent from areas of intestinal metaplasia, even in heavily colonised stomachs (Liu and Crawford, 2005).

There is still a lot we do not know about *H. pylori*. Its exact mechanisms of transmission are unknown and estimated by a process of elimination. It appears to be an intrafamilial gastro-oral or fecal-oral route acquired in childhood from the parents since a lack of acquisition from partners has ruled out the oral-oral route (Perez-Perez *et al.*, 1991), large family size seems to be a predisposing factor (Gao *et al.*, 2010) and child-child transmission in nurseries has not been demonstrated (Tindberg *et al.*, 2001). The relationship between infection and development of complications also varies dramatically according to region where factors such as the virulence of local strains, diet and parasitic infection may play an important role (Tan and Wong, 2011).

Some arguments for a beneficial role of *H. pylori* have also been made. Due to its ability to reduce gastric acid secretion, the reduction in *H. pylori* infection has seen an associated rise in gastro-esophageal reflux disease (GERD) and its associated conditions of Barrett's oesophagus, oesophageal adenocarcinomas and asthma (Blaser, 2006). Children infected with *H. pylori* have lower incidences of diarrhoea compared to the uninfected (Ahmed, 2005) and higher incidences of *H. pylori* infection have also been associated with lower incidences of inflammatory bowel disease, possibly due to its ability to down-regulate the pro-inflammatory responses of the T-cells in the host's gastric mucosa (Yang and Sheu, 2016). Even protective roles in diseases such as metabolic syndrome, type II diabetes and obesity have been postulated due its effect on the expression of leptin and ghrelin, hormones which affect appetite and satiety (Blaser and Atherton, 2004). Whether these benefits outweigh the risks of harbouring a potentially carcinogenic pathogen is subject to debate and there is the possibility that different strains with varying virulence may exist or the relative ease of detection for *H. pylori* makes it an indicator organism for the effects of

the antibiotic age on our microbiome (Blaser, 2006).

### Treatment:

Treatment involves the eradication of *H. pylori* with triple therapy (Clark and Silk, 2002) consisting of two antibiotics and a proton pump inhibitor (PPI) or H<sub>2</sub>-receptor agonist to reduce gastric acid secretion, raising the pH of the stomach to ease discomfort and encourage healing (BNF, 2016). This has almost eliminated the incidence of *H. pylori* in developed countries although rates remain high in other parts of the world and resistance has resulted in the adoption of quadruple therapy, sequential therapy and many other combinations all aimed at the extermination of *H. pylori* (Tan and Wong, 2011). If the dangers and benefits of *H. pylori* have caused controversy then its eradication has been equally controversial with some arguing it should be reserved for those at serious risk (Blaser, 1997) countered with the opinion that it should be made extinct (Graham, 1997). Eradication is still standard practice despite the broad spectrum antibiotics used causing perturbations in the microbial profile of the entire gut associated with metabolic disorders (Yap *et al.*, 2016).

PPIs and H<sub>2</sub>-receptor agonists are also used to treat GERD (BNF, 2016) which may be a side effect of *H. pylori* eradication and may raise the pH of the stomach enough (pH >4) to enable colonisation by microorganisms not naturally occurring (Sheh and Fox, 2016). In particular they may facilitate the movement of surviving *H. pylori* to the areas beyond its usual niche and allow the introduction of nitrosating bacteria that are correlated with gastric cancer. By eradicating *H. pylori* we are replicating some of its effects through pharmacy which may predispose us to the very complications we sought to avoid. Prolonged use of PPIs have even been associated with an increased risk of death from unknown factors (Xie *et al.*, 2017) although increased risk of gastric cancer (Cheung *et al.*, 2017) and cardiovascular complications (Shah *et al.*, 2015; Lazaro *et al.* 2017) have been suggested.

### Chinese Medicine:

Chinese medicine is guided by syndrome differentiation so symptomatic manifestations are required for diagnosis meaning a broader definition than formal histological testing is necessary which includes gastropathy and functional dyspepsia too. Tang *et al.* (2012) describe the main symptoms likely to be

seen as stomach ache (*Weiwantong* 胃脘痛), abdominal distension (*Piman* 痞满) or gastric discomfort (*Caoza* 嘈杂)<sup>1</sup>. They acknowledge there is a difference between symptomatic expression treated by Chinese medicine and *H. pylori* infection diagnosed by laboratory test and advise that when *H. pylori* is present eradication therapy with western medicine should accompany traditional treatment according to syndrome differentiation aimed at alleviating symptoms. Their guidelines and those of Chen and Chen (2015) shall be used to provide a structure for the possible syndromes and recommended formulae. These headings are also agreed upon by Zhang, Zhou et al. (2016) except for the exclusion of yin deficiency, which is notable since they focus on chronic atrophic gastritis for which this is the most common diagnosis in other sources, and damp heat being replaced with phlegm turbidity. Since the aetiology of phlegm is often the stagnation and damage of fluids from pathogenic fire (Clavey, 2002) and the formulas advised such as Warm Gallbladder Decoction (*wen dan tang*) and Sweet Wormwood and Scutellaria Decoction to Clear the Gallbladder (*hao qin qing dan tang*) are also applicable to phlegm syndromes, these may be considered a different classification of the same pattern. One notable omission from all the guidelines was an excess pattern of cold in the stomach. This is probably because it occurs in acute situations and is treated mainly with single herbs or two herb combinations added to formulas aimed at the underlying pattern so will be discussed under individual herbs and modifications.

Additional research for each syndrome was acquired by searching against the University of Westminster database for articles using the formula name and the terms “gastritis”, “dyspepsia”, “peptic ulcer” and “pylori”. They also acknowledge the necessity of customising formulae to the individual so an additional section describing individual herbs that can be added will be included after the discussion of whole formulae. A description of each syndrome can be found at the end of the article.

### Spleen and Stomach Deficiency:

This can be further divided into Spleen and Stomach qi deficiency and Spleen and Stomach deficiency cold.

For Stomach and Spleen qi deficiency Tang et al. (2012) recommend Six-Gentlemen Decoction with Aucklandia and Amomum (*xiang sha liu jun zi tang*), Tonify the Middle to Augment the Qi Decoction (*bu zhong yi qi tang*) or Ginseng Poria, and White Atractylodes Powder (*shen ling bai zhu san*) while Chen and Chen (2015) agree

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with only *xiang sha liu jun zi tang*. Xiao et al. (2012) reviewed Six-Gentlemen Decoction (*liu jun zi tang*) and *xiang sha liu jun zi tang* and decided it might be more effective than prokinetic drugs in functional dyspepsia but that methodology was poor and larger, more rigorously conducted trials are necessary. If believed this would indicate an improvement in symptoms, even if eradication of *H. pylori* is not demonstrated and explains *xiang sha liu jun zi tang* being the second most common formula prescription for peptic ulcer in Taiwan (Huang et al., 2015). Kuriowa et al. (2004) reported that *bu zhong yi qi tang* boosted the immunological function of Natural Killer cells in elderly people and Li et al. (1999) found that it restored anti-tumour responses of stress suppressed T-cells in mice. These suggest a mechanism by which this formula may be effective against *H. pylori* or prevent its progression to neoplasms but neither tested against gastritis specifically. *Shen ling bai zhu san* was only found to be tested for its antacid properties in an artificial stomach model where it was found to have greater acid neutralising properties than water, equivalent to sodium bicarbonate but poorer than colloidal aluminium phosphate (Wu, Chen and Chen, 2010).

For Spleen and Stomach deficiency cold Tang et al. (2012) recommend Astragalus Decoction to Construct the Middle (*huang qi jian zhong tang*) or Regulate the Middle Pill (*li zhong wan*) while Chen and Chen (2015) identify this pattern with peptic ulcers and agree with both formulae. A review of Chinese and English trials found *huang qi jian zhong tang* improved the effectiveness of conventional medicine in both superficial and atrophic gastritis by improving the effect of antibiotics with no serious adverse effects but methodological quality was poor which prevented these conclusions being confirmed (Wei et al., 2015). No studies into *li zhong wan* were found.

## Disharmony of Liver and Stomach:

This disorder can also be divided into two more specific syndromes of Liver invading Stomach or stagnant heat in the Liver and Stomach. There is often an emotional component in these syndromes (Tang *et al.*, 2012) making them more likely to be functional dyspepsia than *H. pylori* infection.

For Liver invading Stomach patterns Frigid Extremities Powder (*si ni san*), Bupleurum Powder to Dredge the Liver (*chai hu shu gan san*) and Minor Bupleurum Decoction (*xiao chai hu tang*) are advised by Tang *et al.* (2012) with Chen and Chen (2015) agreeing with *chai hu shu gan san* for both gastritis and peptic ulcers. Ling *et al.* (2015) looked at the effectiveness of *si ni san* in both upper and lower gastrointestinal disorders to discuss the reasons why a single formula may be effective in different disorders. They suggested it affected common mechanisms found throughout the GI tract such as sphincter and smooth muscle contractions, irritable stimulation and microcirculation but called for higher quality of trials before they could draw firm conclusions. Ohta *et al.* (2006) examined irritable stimulation in greater depth using artificially induced gastric mucosal lesions in rats and found that *si ni san* attenuated the damage caused by neutrophil infiltration and lipid peroxidation with a dose dependent relationship but their acute chemically induced model may not be representative of the chronic bacterially mediated cases most often seen in clinic. Qin, Liu and Yuan (2013) found *chai hu shu gan san* more effective than conventional treatment, although again, concluded methodological quality was low. No specific studies into *xiao chai hu tang* on gastritis, dyspepsia, peptic ulcer or *H. pylori* were found.

For stagnant heat in the Liver and Stomach *hua gan tang*<sup>2</sup>, Augmented Rambling Powder (*jia wei xiao yao san*) or Left Metal Pill (*zuo jin wan*) are recommended by Tang *et al.* (2012) with Chen and Chen (2015) identifying this pattern with peptic ulcers and recommending *zuo jin wan* only. No research or even a complete formula for *hua gan tang* was found but *jia wei xiao yao san* was found to improve symptoms and improve gastric motility in patients with functional dyspepsia (Qu *et al.*, 2009) and a review of 14 other trials also found it to be effective for functional dyspepsia although methodological quality in all was low (Qin, Huang and Ren, 2009). *Zuo jin wan* has demonstrated the inhibition of several inflammatory mediators in mice (Wang *et al.*, 2012; Wang *et al.*, 2015) which may suggest a mechanism by which it could have moderating effect in gastritis.

## Stomach Yin Deficiency:

Tang *et al.* (2012) treat this pattern with Linking Decoction (*yi guan jian*), Benefit the Stomach Decoction (*yi wei tang*) or Ophiopogonis Decoction (*mai men dong tang*). Chen and Chen (2015) prefer to use *mai men dong tang* in cases of gastritis and *yi guan jian* in peptic ulcer disease. Research into *yi guan jian* seemed to focus on hepatic disorders and nothing was found on *yi wei tang* although it is the formula of choice for Maclean and Lyttleton (2002) for this type of gastritis too. *Mai men dong tang* only produced results for antitussive effects and so no conclusions about the efficacy of these formulae could be ascertained.

## Spleen and Stomach Damp-Heat:

The main formulae advised by Tang *et al.* (2012) are Pinellia Decoction to Drain the Epigastrium (*ban xia xie xin tang*), *wen dan tang*, Three-Seed Pill (*san ren tang*), Coptis and Magnolia Bark Drink (*lian po yin*) or Sweet Wormwood and Scutellaria Decoction to Clear the Gallbladder (*hao qin qing dan tang*). Chen and Chen (2015) only recommend *wen dan tang* for this pattern of gastritis although their summary of clinical trials for *ban xia xie xin tang* includes many demonstrating effects in both gastritis and peptic ulcer disease. It was also found to be the most popular formula for peptic ulcers in Taiwan (Huang *et al.*, 2015). Zhao *et al.* (2013) found a modified *ban xia xie xin tang* to be effective compared against placebo in a double-blind RCT for functional dyspepsia but it was diagnosed as “cold and heat in complexity syndrome” rather than Spleen and Stomach damp heat<sup>3</sup>. They also mention previous studies that found *ban xia xie xin tang* to be effective against *H. pylori* but only two of those were available in English and one cited three herbs that are not in *ban xia xie xin tang* as effective against *H. pylori*: *jue ming zi* (*Cassia obtusifolia*), *zhe bei mu* (*Fritillaria thunbergii*) and *ding xiang* (*Eugenia caryophyllata*) (Li *et al.*, 2005) while the other used microcalorimetry coupled with chemometric techniques to test the effect of *huang lian* (*Coptis chinensis*) on *E. Coli* and not *H. pylori* (Kong *et al.*, 2011). No results were found for the remaining formulae.

## Blood Stasis in the Stomach:

For this pattern Tang *et al.* (2012) use Drive Out Stasis from the Mansion of Blood Decoction (*xue fu zhu yu tang*), Sudden Smile Powder (*shi xiao san*) or Salvia Drink (*dan shen yin*). Chen and Chen (2015) agree with *shi xiao san* and *dan shen yin*. There was no research on

any of these formulae for the search terms used. *Shi xiao san* cannot be used in the UK due to it consisting of only two ingredients of which one, *wu ling zhi* (*Trogopterori Faeces*), is an animal product and so does not conform to the UK definition of herbal medicine (Medicines Act, 1968). Maclean and Lyttleton (2002) recommend combining this and *dan shen yin* together so an alternative option may be to add the other ingredient *pu huang* (*Typha angustifolia*) and perhaps another blood mover to *dan shen yin*. Zhang, Tao *et al.* (2016) carried out research into San He Tang which combines *dan shen yin* with Galangal and Cyperus Pill (*liang fu wan*) and *bai he tang*<sup>4</sup>. They discovered this formula targets pathways common to cardiovascular and gastrointestinal disorders making it a good choice where blood stasis is affecting both Heart and Stomach. *xue fu zhu yu tang* is primarily used for cardiovascular disorders too so may also be working on mechanisms common to both disorders but since they do not share any of the same herbs this can only be speculated at present.

### Individual Herbs and Modifications:

Herbs that show a particular action or efficacy against gastritis, dyspepsia or *H. pylori* are suitable for additions to the standard formulae. The herbs mentioned by Li *et al.* (2005) already give three possibilities tested in vitro: *jue ming zi*, *zhe bei mu* and *ding xiang*. In vitro does not always mean effectiveness in humans but Maclean and Lyttleton (2002) advise the addition of *ding xiang* and *bai dou kou* (*Amomum krervanh*) to *li zhong wan* for Stomach yang deficiency cold patterns. For further information on individual herbs, the same database collection was searched for “Chinese herbs” and “gastritis”, “dyspepsia”, “peptic ulcer” or “pylori” and scanned for results that looked at actions of single herbs or pairs.

Shi *et al.* (2011) looked at the inhibition of urease with the extracts of 15 Chinese herbs. Urease plays a key role in the ability of *H. pylori* to colonise the stomach (Sheh and Fox, 2013) so its inhibition may be useful to prevent its colonisation without the global harm to the microbiome caused by antibiotics. *Hou po* (*Magnolia officinalis*) was most effective followed by *jue ming zi* (also mentioned by Li *et al.*, 2005, above) and *huang qin*, however, these were extracted by alcohol and their effect was considerably reduced with water extraction as Chinese herbs are generally delivered. The most effective herb from water extraction was *yan hu suo* (*Corydalis yanhusuo*) which is known for its ability to stop pain in both traditional lore (Bensky *et al.*, 2004) and supported

by modern research (Zhang *et al.*, 2014) suggesting a suitable addition in instances where pain and *H. pylori* are significant factors such as peptic ulcer blood stasis patterns or as the replacement for *wu ling zhi* in *shi xiao san*.

Wang and Huang (2005) screened Taiwanese folk medicines for anti-*H. pylori* effects. They also extracted using alcohol and gave only Latin names so their Chinese translations had to be cross-referenced. Of the five they found strongly effective only two have an entry in the English materia medica (Bensky *et al.*, 2004). These are *Alpinia species root*, which is most likely *Alpinia officinarum Rhizoma*, or *gao liang jiang* which has indications for warming the Stomach, dispersing cold, stopping pain and directing rebellious qi downwards. This makes it a suitable addition to a Spleen and Stomach deficiency cold pattern, or an excess cold condition which was not included in most of the reviews of common patterns but is included by Maclean and Lyttleton (2002) who advise *liang fu wan* for this presentation of gastritis. The other is *Bombax malabaricum* root, which is listed as *mu mian* but only gives the bark (*pi*) and not the root form tested in the study although it does include indications for chronic gastritis and peptic ulcers (Bensky *et al.*, 2004). Of the two they found most effective *Plumbago zeylanica* is not listed at all and *Paederia scandens* only listed as an adulterant of *qing feng teng* (*Sinomenium acutum*). TCMwiki.com (2012a,b) is the only place that lists these herbs as an actual medicine making them unlikely to be of use in clinical practice unless their popularity increases. A second study of prescription patterns in Taiwan (Huang *et al.*, 2015) found the most popular single herb was *hai piao xiao* (*Sepia Endoconcha*) which cannot be used in the UK due to restrictions on animal products (Medicines Act, 1968), followed by *yan hu suo*, *bai ji* (*Bletilla striata*), *bei mu*, *da huang* (*Rheum palmatum*), *hou po* (*Magnolia officinalis*), *dan shen* (*Salvia miltiorrhiza*), *mu xiang* (*Aucklandia lappa*), *chuan lian zi* (*Melia toosendan*) and *sha ren* (*Amomum villosum*). The most popular formula with modification overall was *ban xia xie xin tang* with *yan hu suo*, *bei mu* and *chuan lian zi*. Only frequency of use was determined by this study and efficacy or potential mechanisms require further research although some have already been discussed above. Their claim that TCM users had lower expenditure has to be offset against them also being younger and with fewer comorbidities. This is surprising since the studies of Zhang, Tao *et al.* (2015) and Ling *et al.* (2015) suggested herbal formulas act on common mechanisms of multiple conditions and may be especially well suited to people with the relevant comorbidities.

Two studies looked at *niu bang zi* (*Arctium lappa*) essence as an adjuvant to gastric ulcer treatments. Liu *et al.* (2012) compared *niu bang zi* against a mixture of *dang gui* (*Angelica sinensis*), *zi cao* (*Arnebia eichroma*) and sesame oil when combined with antibiotics to reveal a significant improvement for the *niu bang zi* group. Both *niu bang zi* and *zi cao* are more noted for their ability to vent rashes and clear toxic heat with neither having a traditional application for Stomach disorders, *zi cao* even being contraindicated for spleen deficiency with cold patterns (Bensky *et al.*, 2004) and recently withdrawn from internal use over concerns of pyrrolizidine alkaloids (RCHM, 2016). This makes them a curious pair to choose, possibly conflating all gastric inflammation as toxic heat rather than conducting a traditional pattern diagnosis. They also stress that *niu bang zi* has anti-viral effects when *H. pylori* is a bacteria. Wu *et al.* (2010) looked at *niu bang zi* to promote mucosal repair in ulcer patients and found greater improvement in the active group to the control but they do not explain why there was a 3:1 ratio of active to controls and provided no statistical analysis. In their conclusion, they recommend healthy individuals take burdock essence as a preventative revealing a motive for bias in the desire to market a supplement to a mass audience.

## Conclusions

It is interesting to see the modern arguments regarding *H. pylori* adopting an ecological model of the human being similar to those in Chinese medicine which see the body as a community (e.g. *Su Wen* Ch.8: Unschuld and Tessenow, 2011) or a landscape (e.g. *Neijing Tu*: Pregradio, 2015) to be cultivated and balanced. The mechanisms of Chinese herbs to inhibit the growth of *H. pylori* instead of eradicating it completely might also be of interest to achieve this goal. Meanwhile Chinese researchers are using modern techniques to find biomarkers for different syndrome presentations of gastritis using systems biology (Li *et al.*, 2013) which may help in future trials where objective differentiation of syndromes has always presented a problem. This and other methodological problems make firm conclusions difficult but it seems likely that, with correct differentiation, Chinese herbs can help to favourably influence the outcome of patients with gastritis.

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## Footnotes

**1. Caoza**, 嘈杂, literally means a “noisy crowd” and describes a busy, noisy environment but appears as a chapter heading in Dan Xi’s Jin-Yuan Dynsasty work, *Dan Xi Zhi Fa Xin Yao* (Heart and Essence of Dan Xi’s Treatment Methods). Yang (1993, p161) translates this as “Clamoring Stomach” and being due to phlegm formed from food stagnation and heat. Sionneau and Gang (1998) describe the symptoms as:

“a sensation of emptiness and burning in the stomach duct or heart region which is described as being like hunger but not hunger, like pain but not pain. Typically it is also accompanied by belching, nausea, acid regurgitation and fullness.” (Sionneau and Gang, 1998, p327)

The use of a term for a noisy crowd being applied to gastric discomfort brings to mind the description of the Spleen in the Book of the Centre, also known as the Jade Calendar (in Schipper 1993, p106) as “the Yellow Court, the body’s ritual area and the meeting place of its inhabitants” like a market place where food and services are exchanged becoming overcrowded and raucous.

## 2 Hua gan tang

The ingredients given by Tang *et al.* (2012) are: *Qing pi* (*Citrus reticulata*), *zhi zi* (*Gardenia jasminoides*), *chen pi* (*Citrus Reticulata*), *ze xie* (*Alisma orientalis*), *bai shao* (*Paeonia lactiflora*), *bei mu*, *mu dan pi* (*Paeonia suffruticosa*)

**3. Huang (2009)** discusses the symptomatic presentation of this cold and heat in complexity syndrome in relation to *ban xia xie xin tang*: “These mixed cold-heat patterns can manifest as epigastric focal distention, abdominal fullness and distention that is aggravated when encountering cold, thirst with a lack of desire to drink, dry lips, and a red tongue with a yellow coating. It also can be seen as epigastric focal distention with pain where encountering either cold or heat both increase the patient’s discomfort. The bowels can be either constipated or loose, and the urine can be either yellow or clear.” (Huang, 2009, p265)

From this description there is some overlap with a damp heat presentation but it is not the same and should probably constitute another possible presentation of gastritis.

## 4. Bai He Tang: (Jiao, 2003)

*Bai he* (*Lilium lancifolium*)30g, *wu yao* (*Lindera aggregata*) 9g

## Syndrome Differentiation of Gastritis

Descriptions are taken from Tang *et al.* (2012, 57-58).

### Spleen and Stomach Qi deficiency

“Epigastric distending pain, distention and fullness, weakness and lassitude, aggravation by exertion or exposure to cold, loss of appetite, abdominal distension after meal, sallow or lusterless complexion, loose stool, light red or pale tongue, white or white thin coating, and deep, thread and weak pulse.”

### Spleen and Stomach Deficiency-Cold

“Dull pain of Stomach, preference for warmth and pressure, being ameliorated after meal, fear of cold, cold extremities, clear watery vomit, diarrhea with undigested food, pale, enlarged and teeth-printed tongue, white and slippery coating, and deep and thin, or deep and moderate pulse.”

### Liver qi invading Stomach

“Epigastric distending pain or radiating to costal regions, frequent belching, being aggravated by emotional upset, light red or red tongue, white thin or yellowish thin coating, stringy pulse.”

### Stagnant heat in Liver and Stomach

“Epigastric burning pain, urgent pain, restlessness and irritability, gastric discomfort, acid regurgitation, dry mouth, bitter taste, constipation, red tongue, yellow coating, and rapid stringy pulse.”

### Stomach-Yin Deficiency

“Epigastric burning pain, hunger without desire to eat, dry mouth, constipation, red and dry tongue, less or no coating or with fissures, and rapid thin or stringy thin pulse.”

### Spleen and Stomach Damp-Heat

“Burning sensations, distending pain, and pain in the epigastric region, resistance to pressing, distention and fullness in stomach, heaviness and weakness of limbs, bitter taste and stickiness in mouth, halitosis, thirsty without polydipsia, anorexia, nausea, sticky and stagnant feeling in defecation, red tongue, yellowish thick or thick greasy coating, and slippery or rapid soft pulse.”

### Blood Stasis in Stomach collaterals

“Epigastralgia, fixed or prolonged pain, resistance to pressure, melena, dark red or purplish tongue with ecchymosis or petechiae, stasis or expansion of sublingual vessels, and moderate, astringent and stringy pulse.”

## References

Ahmed, N. (2005) 23 years of the discovery of *Helicobacter pylori*: Is the debate over? *Annals of Clinical Microbiology and Antimicrobials* 4:17. Available from <http://dx.doi.org/10.1186/1476-0711-4-17> [Accessed 15-5-16].

Beers, M.H. and Berkow, R. (2004). *The Merck Manual of Diagnosis and Therapy*, 17th Edition. Whitehouse Station: Merck Research Laboratories.

Bensky, D., Clavey, S., Stöger, E. and Gamble, A. (2004). *Chinese Herbal Medicine: Materia Medica*. 3rd Edition. Seattle, WA: Eastland Press.

Blaser, M.J. (1997). Not all *Helicobacter pylori* strains are created equal: should all be eliminated? *The Lancet* 349 (9057), 1020–22. Available from [http://dx.doi.org/10.1016/S0140-6736\(96\)09133-7](http://dx.doi.org/10.1016/S0140-6736(96)09133-7) [Accessed 5-6-16].

Blaser, M.J. (2006). Who are we? Indigenous microbes and ecology of human diseases. *European Molecular Biology Organisation Reports* 7(10), 956-960. Available from: <http://dx.doi.org/10.1038/>

<http://dx.doi.org/10.1038/sj.embor.7400812> [Accessed 5-6-16].

Blaser, M.J. and Atherton, J.C. (2004). *Helicobacter pylori* persistence: biology and disease. *The Journal of Clinical Investigation* 113(3), 321-333. Available from <http://dx.doi.org/10.1172/JCI20925> [Accessed 5-6-16].

BNF (2016). 1.3 Antisecretory drugs and mucosal protectants. *British National Formulary*. Available from <http://www.evidence.nhs.uk/formulary/bnf/current/1-gastro-intestinal-system/13-antisecretory-drugs-and-mucosal-protectants> [Accessed 6-6-16].

Chen J.K. and Chen, T.T. (2015). *Chinese Herbal Formulas and Applications: Pharmacological Effects and Clinical Research*. City of Industry: Art of Medicine Press.

Cheung, K.S., Chan, E.W., Wong, A.Y.S., Chen, L., Wong, I.C.K. and Leung, W.K. (2017). Long-term proton pump inhibitors and risk of gastric cancer development after treatment for *Helicobacter pylori*: a population-based study. In *Gut* Published Online First: 31 October 2017. Available from: <http://dx.doi.org/10.1136/gutjnl-2017-314605> [Accessed 1-11-17].

Clark, M.L. and Silk, D.B. (2002). Gastrointestinal disease. In: Kumar, P. and Clark M. (eds) *Clinical Medicine* 5th Edition. Bath: WB Saunders, 253-334.

Clavey, S. (2002). *Fluid Physiology and Pathology in Traditional Chinese Medicine*, 2nd Edition. China: Churchill Livingstone.

Du L.J., Chen B.R., Kim J.J., Kim S., Shen J.H., Dai N. (2016) *Helicobacter pylori* eradication therapy for functional dyspepsia: Systematic review and meta-analysis. *World Journal of Gastroenterology* 22(2), 3486-3495. Available from <http://dx.doi.org/10.3748/wjg.v22.i2.3486> [Accessed 5-6-16].

Gao, L., Weck, M.N., Raum, E., Stegmaier, C., Rothenbacher, D. and Brenner, H. (2010). Sibship size, *Helicobacter pylori* infection and chronic atrophic gastritis: a population-based study among 9444 older adults from Germany. *International Journal of Epidemiology* 39(1), 129-134. Available from <http://dx.doi.org/10.1093/ije/dyp250> [Accessed 6-6-16].

Graham, D.Y. (1997). The only good *Helicobacter pylori* is a dead *Helicobacter pylori*. *The Lancet* 350 (9070), 70. Available from [http://dx.doi.org/10.1016/S0140-6736\(05\)66278-2](http://dx.doi.org/10.1016/S0140-6736(05)66278-2) [Accessed 5-6-16].

Huang, H. (2009). *Ten Key Formula Families in Chinese Medicine*. Translated by Michael Max. Seattle, WA: Eastland Press.

Huang, C-Y., Lai, W-Y., Sun, M-F., Lin, C-C., Chen, B-C., Len, H-J., Chang, C-M., Yang, C-H., Huang, K-C. and Yen, H-R. (2015). Prescription patterns of traditional Chinese medicine for peptic ulcer disease in Taiwan: a nationwide population based study. *Journal of Ethnopharmacology* 176 (2015), 311-320. Available from: <http://dx.doi.org/10.1016/j.jep.2015.11.002> [Accessed 29-8-17].

Jiao, S-D. (2003): *Ten Lectures on the Use of Medicinals from the Personal Experience of Jiao Shu-De*. Taos, NM: Paradigm Publications.

Kong, W., Wang, J., Xiao, X., Chen, S. and Yang, M. (2012). Evaluation of antibacterial effect and mode of *Coptidis rhizoma* by microcalorimetry coupled with chemometric techniques. *Analyst* 137(1), 216–222. Available from <http://dx.doi.org/10.1039/c1an15826k> [Accessed 11-6-16].

Kuepper-Nybelen, J., Rothenbacher and Brenner, H. (2005). Relationship between Lifetime Alcohol Consumption and *Helicobacter pylori* Infection. *Annals of Epidemiology* 15(8), 607-613. Available from <http://dx.doi.org/10.1016/j.annepidem.2004.11.001>

[Accessed 6-6-16].

Kuroiwa, A., Liou, S., Yan, H., Eshita, A., Naitoh, S. and Nagayama, A. (2004). Effect of a traditional Japanese herbal medicine, *Hochu-ekki-to* (*Bu-Zhong-Yi-Qi Tang*), on immunity in elderly persons. *International Immunopharmacology* 4, 317 – 324. Available from <http://dx.doi.org/10.1016/j.intimp.2003.12.004> [Accessed 10-6-16].

Lázaro, A.M.P., Cristóbal, C., Franco-Peláez, J.A., Tarín, N., Aceña, A., Carda, R., Huelmos, A., Martín-Mariscal, M.L., Fuentes-Antras, J., Martínez-Millá, J., Alonso, J., Lorenzo, O., Egado, J., López-Bescós, L., Tuñón, J. (2017). Use of Proton-Pump Inhibitors Predicts Heart Failure and Death in Patients with Coronary Artery Disease. In *PLoS One* 12(1): e0169826. Available from: <https://doi.org/10.1371/journal.pone.0169826> [Accessed 1-11-17].

Li, R., Ma, T., Gu, J., Liang, X. and Li, S. (2013). Imbalanced network biomarkers for traditional Chinese medicine Syndrome in gastritis patients. *Scientific Reports* 3:1543. Available from: <http://dx.doi.org/10.1038/srep01543> [Accessed 12-6-16].

Li, T., Tamada, K., Abe, K., Tada, H., Onoe, Y., Tatsugami, K., Harada, M., Kubo, C. and Nomoto, K. (1999). The restoration of the antitumor T cell response from stress-induced suppression using a traditional Chinese herbal medicine *Hochu-ekki-to* (TJ-41: *Bu-Zhong-Yi-Qi-Tang*). *Immunopharmacology* 43, 11–21. Available from [http://dx.doi.org/10.1016/S0162-3109\(99\)00034-X](http://dx.doi.org/10.1016/S0162-3109(99)00034-X) [Accessed 11-6-16].

Li, Y., Xu, C., Zhang, Q., Liu, J.Y. and Tan, R.X. (2005). In vitro anti-*Helicobacter pylori* action of 30 Chinese herbal medicines used to treat ulcer diseases. *Journal of Ethnopharmacology* 98(3), 329–333. Available from <http://dx.doi.org/10.1016/j.jep.2005.01.020> [Accessed 11-6-16].

Ling, W., Li, Y., Jiang, W., Sui, Y. and Zhao H-L. (2015). Common Mechanism of Pathogenesis in Gastrointestinal Diseases Implied by Consistent Efficacy of Single Chinese Medicine Formula. A PRISMA-Compliant Systematic Review and Meta-Analysis. *Medicine* (Baltimore) 94(27): e1111. Available from <http://dx.doi.org/10.1097%2FMD.0000000000001111> [Accessed 11-6-16].

Liu, C. and Crawford, J.M. (2005). The Gastrointestinal Tract. In: Kumar, V., Abbas, A.K. and Fausto, N. (eds) *Robbins and Cotran Pathologic Basis of Disease*, 7th Edition. Philadelphia: Elsevier Saunders, 797-875.

Liu, H-C., Ku, M-K., Chung, F-Y., Lin, C-C. And Lin, S-R. (2012). Effectiveness of great burdock essence compounds in the adjuvant treatment of gastric ulcer patients infected with *Helicobacter pylori*. *Genomic Medicine, Biomarkers, and Health Sciences* 4, 81-84. Available from: <http://dx.doi.org/10.1016/j.gmbhs.2012.09.001> [Accessed 15-5-16].

Maclean, W. and Lyttleton, J. (2002). *Clinical Handbook of Internal Medicine. The Treatment of Disease with Traditional Chinese Medicine*. Volume 2: Spleen and Stomach. Sydney: University of Western Sydney.

Marshall, B.J., Armstrong, J.A., McGeachie, D.B., Glancy, R.J. (1985). Attempt to fulfil Koch's postulates for *pyloric campylobacter*. *Medical Journal of Australia* 142, 436-439. Available from: [http://www.med.mcgill.ca/epidemiology/hanley/c609/material/AmeeM/Marshall\\_Koch\\_Hpylori\\_1985.pdf](http://www.med.mcgill.ca/epidemiology/hanley/c609/material/AmeeM/Marshall_Koch_Hpylori_1985.pdf) [Accessed 5-6-16].

Marshall, B.J., and Warren, J.R. (1984). Unidentified Curved Bacilli in the Stomach of Patients with Gastritis and Peptic Ulceration. *The Lancet* 323 (8390), 1311-1315. Available from: [http://dx.doi.org/10.1016/S0140-6736\(84\)91816-6](http://dx.doi.org/10.1016/S0140-6736(84)91816-6) [Accessed 5-6-16].

*Medicines Act 1968*. Chapter 67. London: Department of Health. Available from <http://www.legislation.gov.uk/ukpga/1968/67>

[Accessed 12-6-16].

Nardone, G. and Compare, D. (2015). The human gastric microbiota: Is it time to rethinking the pathogenesis of stomach diseases? *United European Journal of Gastroenterology* 3(3), 255-260. Available from <http://dx.doi.org/10.1177/2050640614566846> [Accessed 5-6-16].

NHS Choices (2014). *Gastritis*. Available from <http://www.nhs.uk/conditions/gastritis/Pages/Introduction.aspx> [Accessed 5-6-16].

Ohta, Y., Kobayashi, T., Hayashi, T., Inui, K., Yoshino, J. and Nakazawa, S. (2006). Preventative Effect of *Shigyaku-san* on Progression of Acute Gastric Mucosal Lesions Induced by Compound 48/80, a Mast Cell Degranulator, in Rats. *Phytotherapy Research* 20, 256-262. Available from: <http://dx.doi.org/10.1002/ptr.1832> [Accessed 30-8-17].

Perez-Perez, G.I., Witkin, S.S., Decker, M.D., Blaser, M.J. (1991). Seroprevalence of *helicobacter pylori* infection in couples. *Journal of Clinical Microbiology* 29(3), 642-644. Available from <http://jcm.asm.org/content/29/3/642> [Accessed 6-6-16].

Planeta Verde (2016). Hua Gan Tang. *Planeta Verde*. Available from <http://www.planetaverd.ad/en/product/view/4839CD1E-2EEB-4852-AD9C-FE9640A091B3> [Accessed 12-6-16].

Pregradio, F. (2015). Neijing Tu (Chart of the Inner Warp). *The Golden Elixir*. Available from [http://www.goldenelixir.com/jindan/neijing\\_tu.html](http://www.goldenelixir.com/jindan/neijing_tu.html) [Accessed 12-6-16].

Qin, F., Huang, X. and Ren, P. (2009). Chinese herbal medicine modified xiaoyao san for functional dyspepsia: Meta-analysis of randomised controlled trials. *Journal of Gastroenterology and Hepatology* 24, 1320-1325. Available from <http://dx.doi.org/10.1111/j.1440-1746.2009.05934.x> [Accessed 11-6-16].

Qin, F., Liu, J-Y. and Yuan, J-H. (2013). Chaihu-Shugan-San, an oriental herbal preparation, for the treatment of chronic gastritis: A meta-analysis of randomized controlled trials. *Journal of Ethnopharmacology* 146, 433–439. Available from <http://dx.doi.org/10.1016/j.jep.2013.01.029> [Accessed 11-6-16].

Qu, Y., Gan, H.Q., Mei, Q.B. and Liu, L. (2010). Study on the Effect of Jia-Wei-Xiao-Yao-San Decoction on Patient with Functional Dyspepsia. *Phytotherapy Research* 24, 245-248. Available from <http://dx.doi.org/10.1002/ptr.2920> [Accessed 11-6-16].

RCHM (2016). *TAKE ACTION ON THIS ADVICE* - continued restriction on herbs containing pyrrolizidine alkaloids (Pas). [email]. Sent to Steve Woodley, 21 August.

Scheid, V., Bensky, D., Ellis, A. and Barolet, R. (2009). *Chinese Herbal Medicine: Formulas and Strategies*. 2Nd Edition. Seattle, WA: Eastland Press.

Schipper, K. (1993). *The Taoist Body*. Translated by Duval, K.C. Berkeley: University of California Press.

Shah, N-H., LePendou, P., Bauer-Mehren, A., Ghebremariam, Y.T., Iyer, S.V., Marcus, J., Nead, K.T., Cooke, J.P., Leeper, N.J. (2015). Proton Pump Inhibitor Usage and the Risk of Myocardial Infarction in the General Population. In *PLoS One* 10(6): e0124653. Available from: <https://doi.org/10.1371/journal.pone.0124653> [Accessed 1-11-17].

Sheh, A. and Fox, J.G. (2013). The role of the gastrointestinal microbiome in *Helicobacter pylori* pathogenesis. *Gut Microbes* 4(6), 505-531. Available from <http://dx.doi.org/10.4161/gmic.26205> [Accessed 15-5-16].

Shi, D-H., Liu, Y-W., Liu, W-W. and Gu, Z-F. (2011). Inhibition of urease by extracts derived from 15 Chinese medicinal herbs.

- of urease by extracts derived from 15 Chinese medicinal herbs. *Pharmaceutical Biology* 49(7), 752–755. Available from: <http://dx.doi.org/10.3109/13880209.2010.547205> [Accessed 12-6-16].
- Sionneau, P. and Gang, L. (1998). *The Treatment of Disease in TCM vol. 5: Diseases of the Chest, Abdomen and Rib Side*. Boulder, CO: Blue Poppy Press.
- Tan, V.P.Y. and Wong, B.C.Y. (2011). *Helicobacter pylori* and gastritis: Untangling a complex relationship 27 years on. *Journal of Gastroenterology and Hepatology* 26, Suppl. 1, 42–45.
- Tang, X-D., Lu, B., Zhou, L-Y., Zhan, S-Y., Li, Z-H., Li, B-S., Gao, R., Wang, F-Y., Wang, P., Tang, J-Q., Liu, G., Zhang, Y-Q., Che, G-X., Lin, M., Bian, L-Q. and Zhao, Y-P. (2012). Clinical Practice Guideline of Chinese Medicine for Chronic Gastritis. *Chinese Journal of Integrative Medicine* 18(1), 56–71. Available from <http://dx.doi.org/10.1007/s11655-012-0960-y> [Accessed 11-6-16].
- TCMwiki.com (2012a). *Ji Shi Teng*. TCM Wiki. Available from <http://old.tcmwiki.com/wiki/ji-shi-teng> [Accessed 12-6-16].
- TCMwiki.com (2012b). *Bai Hua Dan*. TCM Wiki. Available from [http://www.tcmwiki.com/w/Bai\\_Hua\\_Dan](http://www.tcmwiki.com/w/Bai_Hua_Dan) [Accessed 12-6-16].
- Tindberg, Y., Bengtsson, C., Granath, F., Blennow, M., Nyrén, O., Granström, M. (2001). Helicobacter pylori Infection in Swedish School Children: Lack of Evidence of Child-to-Child Transmission Outside the Family. *Gastroenterology* 121 (2), 310–316. Available from <http://dx.doi.org/10.1053/gast.2001.26282> [Accessed 6-6-16].
- Unschuld, P.U. and Tessenow, H. (2011). *Huang Di Nei Jing Su Wen. An annotated Translation of Huang Di's Inner Classic – Basic Questions, Volume I, Chapters 1 through 52*. Berkeley, CA: University of California Press.
- Wang, Q-S., Cui, Y-L., Dong, T-J., Zhang, X-F. and Lin, K-M. (2012). Ethanol extract from a Chinese herbal formula, "Zuojin Pill", inhibit the expression of inflammatory mediators in lipopolysaccharide-stimulated RAW 264.7 mouse macrophages. *Journal of Ethnopharmacology* 141(1), 377–385. Available from <http://dx.doi.org/10.1016/j.jep.2012.02.049> [Accessed 11-6-16].
- Wang, Y-C. and Huang, T-L. (2004) Screening of anti-Helicobacter pylori herbs deriving from Taiwanese folk medicinal plants. *FEMS Immunology and Medical Microbiology* 43, 295–300. Available from <http://dx.doi.org/10.1016/j.femsim.2004.09.008> [Accessed 15-5-16].
- Wang, J., Zhang, T., Zhu, L., Ma, C. and Wang, S. (2015). Anti-ulcerogenic effect of Zuojin Pill against ethanol-induced acute gastric lesion in animal models. *Journal of Ethnopharmacology* 173, 459–467. Available from <http://dx.doi.org/10.1016/j.jep.2015.04.017> [Accessed 11-6-16].
- Wei, Y., Ma, L-X., Yin, S-J., An, J., Wei, Q. and Yang, J-X. (2015). Huangqi Jianzhong Tang for Treatment of Chronic Gastritis: A Systematic Review of Randomized Clinical Trials. *Evidence-Based Complementary and Alternative Medicine* 2015, Article ID 878164. Available from <http://dx.doi.org/10.1155/2015/878164> [Accessed 11-6-16].
- Wu, T-H., Chen, I-C. and Chen, L-C. (2010). Antacid effects of Chinese herbal prescriptions assessed by a modified artificial stomach model. *World Journal of Gastroenterology* 16(35), 4455–4459. Available from <http://dx.doi.org/10.3748/wjg.v16.i35.4455> [Accessed 11-6-16].
- Wu, Y-C., Lin, L-F., Yeh, C-S., Lin, Y-L., Chang, H-J., Lin, S-R., Chang, M-Y., Hsiao, C-P. and Lee, S-C. (2010). Burdock Essence Promotes Gastrointestinal Mucosal Repair in Ulcer Patients. *Fooyin Journal of Health Sciences* 2(1), 26–31. Available from [http://dx.doi.org/10.1016/S1877-8607\(10\)60010-0](http://dx.doi.org/10.1016/S1877-8607(10)60010-0) [Accessed 15-5-16].
- Xiao, Y., Liu, Y-Y., Yu, K-Q., Ouyang, M-Z., Luo, R. and Zhao, X-S. (2012). Chinese Herbal Medicine Liu Jun Zi Tang and Xiang Sha Liu Jun Zi Tang for Functional Dyspepsia: Meta-Analysis of Randomized Controlled Trials. *Evidence-Based Complementary and Alternative Medicine* 2012, Article ID 936459. Available from <http://dx.doi.org/10.1155/2012/936459> [Accessed 11-6-16].
- Xie, Y., Bowe, B., Li, T., Xian, H., Yan, Y., Al-Aly, Z. (2017). Risk of death among users of Proton Pump Inhibitors: a longitudinal observational cohort study of United States veterans. *BMJ Open* 2017; 7:e015735. Available from: <http://dx.doi.org/10.1136/bmjopen-2016-015735> [Accessed 27-8-17].
- Yang, S-Z. (1993). *The Heart & Essence of Dan-Xi's Methods of Treatment*. A Translation of the Zhu Dan-xi's Dan Xi Zhi Fa Xin Yao. Boulder, CO: Blue Poppy Press.
- Yang, Y-J. and Sheu B-S. (2016). Metabolic Interaction of Helicobacter pylori Infection and Gut Microbiota. *Microorganisms* 4(15). Available from <http://dx.doi.org/10.3390/microorganisms4010015> [Accessed 15-5-16].
- Yap, T. W-C., Gan, H-M., Lee, Y-P, Leow, A. H-R., Azmi, A. N., Francois, F., Perez-Perez, G. I., Loke, M-F., Goh, K-L. and Vadivelu, J. (2016). Helicobacter pylori Eradication Causes Perturbation of the Human Gut Microbiome in Young Adults. *PLoS ONE* 11(3), e0151893. Available from <http://dx.doi.org/10.1371/journal.pone.0151893> [Accessed 15-5-16].
- Zhang, Y., Wang, C., Wang, L., Parks, G.S., Zhang, X., Guo, Z., Ke, Y., Li, K-W., Kim M.K., Vo, B., Borrelli, E., Ge, G., Yang, L., Wang, Z., Garcia-Fuster, M.J., Luo, Z.D., Liang, X. and Civelli, O. (2014). A novel analgesic Isolated from a Traditional Chinese Medicine. *Current Biology* 24(2), 117–123. Available from: <http://dx.doi.org/10.1016/j.cub.2013.11.039> [Accessed 11-8-16].
- Zhang, W., Tao, Q., Guo, Z., Fu, Y., Chen, X., Shar, P.A., Shahan, M., Zhu, J., Xue, J., Bai, Y., Wu, Z., Wang, Z., Xiao, W. and Wang, Y. (2016). Systems Pharmacology Dissection of the Integrated Treatment for Cardiovascular and Gastrointestinal Disorders by Traditional Chinese Medicine. *Scientific Reports* 6 (32400). Available from: <http://dx.doi.org/10.1038/srep32400> [Accessed 27-8-17].
- Zhang, Y., Zhou, A., Liu, Y., Zhao, Y., Zhang, L., Sun, L., Du, S., Yang, Q., Song, X., Liang, C. and Ding, X. (2016). Exploratory Factor Analysis for Validating Traditional Chinese Syndrome Patterns of Chronic Atrophic Gastritis. *Evidence Based Complementary and Alternative Medicine* 2016, Article ID 6872890. Available from: <http://dx.doi.org/10.1155/2016/6872890> [Accessed 27-8-17].
- Zhao, L., Zhang, S., Wang, Z., Wang, C., Huang, S. Shen, H., Wei, W., Wang, H. and Wu, B. (2013). Efficacy of Modified Ban Xia Xie Xin Decoction on Functional Dyspepsia of Cold and Heat in Complexity Syndrome: A Randomized Controlled Trial. *Evidence-Based Complementary and Alternative Medicine* 2013, Article ID 812143. Available from <http://dx.doi.org/10.1155/2013/812143> [Acc Accessed 11-6-16].