Gegen Qinlian Decoction is one of the commonly used classical prescriptions, which consists of four herbs: Gegen (Puerariae Lobatae Radix), Huangqin (Scutellariae Radix), Huanglian (Coptidis Rhizoma), and Zhigancao Glycyrrhizae Radix et Rhizoma Praeparata cum Melle. The clinical application experience of Gegen Qinlian Decoction is as follows: first, according to Zhongjing Zhang’s original text, heat distressing the large intestine with unresolved exterior syndrome is the original meaning of Gegen Qinlian Decoction syndrome. In clinical practice, bacillary dysentery, gastrointestinal cold, etc., belong to simultaneous exterior and interior disease, which are completely consistent with the original meaning of this prescription; second, the clinical digestive system diseases with exuberant heat of the large intestine as the core manifestation cannot be treated merely based on the exterior syndrome; third, due to the interior–exterior relationship between the lung and the large intestine and between the meridians, the use of Gegen (Puerariae Lobatae Radix), Huangqin (Scutellariae Radix), and Huanglian (Coptidis Rhizoma) can make the source of body clear, and the waste qi can be released and the pore can be easily opened, so this prescription can also be used for exogenous fever; fourth, with multidimensional comprehensive understanding of the syndrome, pathogenesis, symptoms and pharmacology, Gegen Qinlian Decoction has also been further applied to the treatment of hypertension, diabetes, etc.

Gegen Qinlian Decoction is derived from section 34 of Treatise on Cold Damage (Shang Han Lun), which says: “When in Taiyang Disease and Guizhi syndrome, the
Physician applies the wrong reverse treatment of purgation method, causing incessant diarrhea and abrupt pulse, which means that the exterior has not resolved. For patients with panting and sweating, Gegen Qinlian Decoction can be chosen. For Taiyang Disease and Guizhi syndrome, the sweating method should be applied. If purgation method is applied, it is an erroneous treatment, so it is named wrong reverse treatment. If the doctor applies the purgation method in this situation, it will impair the stomach and intestine and lead to continuous diarrhea. At this time, the pulse rate will increase. Although the stomach and intestine get impaired, healthy qi can still resist pathogenic qi and the pathogenic factors haven’t entered deep into the body and they can be expelled to the exterior. If the external pathogenic factors haven’t been resolved and internal heat is already exuberant, the external and internal heat will lead to the symptoms of general fever, dysphoric fever in the chest, thirst, red tongue with yellow coating, rapid pulse rate; invasion of the large intestine by heat leads to failure of transmission in the large intestine, which results in acute diarrhea with fetid feces and burning sensation in the anus; the lung and large intestine are related internally and externally, if internal heat steams upward to the lung, it results in uneven unctuning of the lung qi which causes panting, while if it steams externally on the skin, sweating will be caused. Sweating and diarrhea are both pathological manifestations and reactions of pathogenic qi exiting the body.

Gegen Qinlian Decoction not only takes into account internal exuberant pathogenic heat but also considers the elimination of pathogenic qi with the help of healthy qi. In the prescription, Gegen (Puerariae Lobatae Radix) is sweet, pungent in taste, and cold in nature. According to the Miscellaneous Records of Famous Physicians (Ming Yi Bie Lu), “It (Gegen) can be used to treat headache due to stroke, dispel the pathogenic factors from the skin, sweating and opening striae and interstices… treat high fever due to cold damage.” The Treatise on the Properties of the Medicinals (Yao Xing Lun) states that “It (Gegen) can treat upward flow of qi.” In the Treatise on Cold Damage (Shang Han Lun), Gegen Decoction and Guizhi Plus Gegen Decoction are used to treat stiffness of the nape and back; Gegen (Puerariae Lobatae Radix) can enter Taiyang to ventilate meridian qi, relieve the exterior, and expel wind. Gegen (Puerariae Lobatae Radix) can also enter Yangming which governs the stomach from inside and muscles from outside. Therefore, it can ascend the lucid, check diarrhea, and also eliminate pathogenic factors from the muscles. Gegen (Puerariae Lobatae Radix) was commonly used by the doctors of the School of Warm Diseases in the Ming and Qing Dynasties for the treatment of eczema or measles which failed to erupt. Therefore, Gegen (Puerariae Lobatae Radix) itself is a typical herb that can simultaneously enter Taiyang and Yangming meridians and relieve both the exterior and the interior syndromes. Qin Ke believed that it is light in property and heavy in weight. Application of it with large dosage and decoction can make it more effective.

In the prescription, both Huangqin (Scutellariae Radix) and Huanglian (Coptidis Rhizoma) have a bitter taste and cold nature. Cold property can clear heat, and bitter taste can dry dampness, preserve yin, check diarrhea, and strengthen the stomach and intestine. Among them, Huanglian (Coptidis Rhizoma) is the best at clearing gastrointestinal dampness and heat. Shen Nong’s Classic of Materia Medica (Shen Nong Ben Cao Jing) says “Huanglian (Coptidis Rhizoma) is effective on Changpi, abdominal pain and dysentery.” The Miscellaneous Records of Famous Physicians (Ming Yi Bie Lu) says “long-term diarrhea with bloody purulent stool, Huanglian (Coptidis Rhizoma) can be used to regulate stomach and strengthen the large intestine.” Huangqin (Scutellariae Radix) can also clear dampness and heat. The Shen Nong’s Classic of Materia Medica (Shen Nong Ben Cao Jing) records that “It (Huangqin) is effective on jaundice, Changpi, diarrhea and dysentery due to various heat.” The Encountering the Sources of the ‘Classic of Materia Medica’ (Ben Jing Feng Yuan) says “It (Huangqin) is bitter in taste and dry in nature and has the functions to strengthen the intestine and stomach.” The Treatise on Cold Damage (Shang Han Lun) records that “Huangqin Decoction dominates the concurrent disease of both Taiyang and Shao yang meridians with symptom of diarreha”. Huangqin (Scutellariae Radix) and Huanglian (Coptidis Rhizoma) supplement each other to remove gastrointestinal dampness and heat and check diarrhea. Gancao (Glycyrrhizae Radix et Rhizoma) is sweet in taste and mild in nature, which can be used to harmonize all herbs. The combination of the four herbs can disperse the exterior and clear the interior, leading to harmonization between the exterior and interior and soothing general fever and diarrhea.

Gegen Qinlian Decoction syndrome is originally used for heat invading the large intestine and unrelied exterior syndrome. In clinical practice, acute enteritis, bacillary dysentery, enterotrophoid fever, autumn diarrhea in children, gastrointestinal cold, etc., belong to concurrent internal and external diseases, which are completely consistent with the original meaning of this prescription. Therefore, this prescription can be modified for treating these diseases.

**For the Treatment of Diseases Caused by Intestinal Heat**

Although Gegen Qinlian Decoction is for relieving the exterior and clearing the interior and can treat the exterior and interior syndrome simultaneously, it can be seen from the herbs used in this prescription that it is mainly for clearing internal heat and is supplemented by relieving the exterior syndrome and dispersing pathogenic factors. The Yellow Emperor’s Inner Canon (Huang Di Nei Jing) says that “All syndromes characterized by acute diarrhea are associated with heat.” And internal heat and diarrhea should be the main indications and necessary syndrome in this section. In clinical application, it is not limited by the presence or absence of exogenous pathogenic factors. Regardless of the presence or absence of Taiyang exterior syndrome, Gegen Qinlian Decoction can be used for patients with Yangming damp-heat diarrhea.

When the heat in the stomach and intestine is exuberant, Huangqin (Scutellariae Radix) and Huanglian (Coptidis Rhizoma) can be chosen to clear heat, dry dampness, preserve yin, and check diarrhea. In the Treatise on Cold Damage (Shang Han Lun), Huanglian (Coptidis Rhizoma) and Huangqin (Scutellariae Radix) can often be seen as a pair of herbs.
appearing in multiple prescriptions such as Gegen Qinlian Decoction, Banxia Xiexin Decoction, and Ganjiang Huangqin Huanglian Renshen Decoction, which obviously shows that Zhongjing Zhang often used them as the basic compatibility for treating intestinal heat and diarrhea.

In addition, the effects of Gegen (Puerariae Lobatae Radix) for ascending Qingyang, invigorating yang qi of the spleen and stomach to ascend and check diarrhea, should also be valued. Gegen (Puerariae Lobatae Radix) can be used for both deficiency and excess syndromes in the treatment of diarrhea. It can treat both heat and cold syndromes. Dongyuan Li believed that Gegen (Puerariae Lobatae Radix) is "an effective herb for treating spleen deficiency and diarrhea". For example, in the Key to Diagnosis and Treatment of Children's Diseases (Xiao Er Yao Zheng Zhi Jue), Qiwei Baizhu Powder is used in combination with Renshen (Ginseng Radix et Rhizoma), Baizhu (Atractylodis Macrocephalae Rhizoma), Muxiang (Aucklandiae Radix), etc., Gancao (Glycyrrhizae Radix et Rhizoma) is sweet in taste and mild in nature, which can harmonize all herbs. The combination of the four herbs can check diarrhea, sweating, and polydipsia.

The common diseases seen in the clinic, such as acute and chronic gastritis, chronic enteritis, chronic diarrhea, irritable bowel syndrome, ulcerative colitis, etc., with symptoms of diarrhea with fetid and sticky feces, burning sensation of the anus, heat vexation in the chest, dry mouth and thirst, dark urine, red tongue with yellow coating, and slippery and rapid pulse rate, can reflect the core pathogenesis of exuberant heat in the large intestine, so Gegen Qinlian Decoction can be used. It is worth mentioning that for patients with mixed cold and heat syndrome, upper heat and lower cold, this prescription can be used combined with Sishen Pill, Lizhong Decoction, and Fuzi Lизhong Decoction to regulate both cold and heat. As for the dosage, Gegen (Puerariae Lobatae Radix) in the original prescription is 250 g. In modern clinical practice, Gegen (Puerariae Lobatae Radix) should also be used in large dosages to take effect, generally 20–30 g. But if there is no exogenous pathogen and neck and back stiffness, Gegen (Puerariae Lobatae Radix) should not be used in large dosages. The amount equal to Huanglian (Coptidis Rhizoma) and Huangqin (Scutellariae Radix) should be used, generally 10–15 g.

**For the Treatment of Exogenous Heat Syndrome**

The basic treatment for heat syndrome should be the clearing method. However, due to the complexity of the clinical diseases, heat syndromes are also of different types such as exterior, interior, deficiency, or excess syndromes. Therefore, when the clearing method is used to treat heat syndrome, evidence-based flexible therapeutic methods can be effective. Shengbai Xue of the Qing Dynasty once emphasized on the treatment of diarrhea in the chapter of Damp-Heat Disease that "It is necessary to add Jiegeng (Platyctodonis Radix), Xingren (Armeniacae Semen Amarum) and Dadou Huangjuan (Sojae Semen Germinatum) to dredge the middle Jiao and the upper Jiao. Since the source becomes clear, the flow will also be clean."5 It is also conducive to the removal of water dampness in the large intestine by dispersing lung qi and unblocking the upper Jiao. Because of the interior-exterior relationship between the lung and the large intestine and the connections between the meridians, if the dampness heat in the intestine is removed, the accumulation of pathogenic factors in the lung are expelled, and the exogenous pathogenic factors are accordingly released.

For the primary symptoms of the syndrome of Gegen Qinlian Decoction in the items, in addition to diarrhea and irregular-rapid pulse, Zhongjing Zhang also particularly stressed the occurrence of “panting and sweating.” Intestinal heat attacks the lung and induces asthma. Since the lung dominates the skin, hair, and sweating, the bridge of the lung in the interior-exterior relationship is highlighted. In the Gegen Qinlian Decoction, Gegen (Puerariae Lobatae Radix) functions to ascend the lucid and check diarrhea, disperse the lung and guide the pathogenic factors to the exterior; and the use of Huangqin (Scutellariae Radix) is also very ingenious. Huangqin (Scutellariae Radix) is used with the Huanglian (Coptidis Rhizoma) to remove the dampness and heat in the intestine and then combined with Gegen (Puerariae Lobatae Radix) to make the source clear. At the same time, Huangqin (Scutellariae Radix) directly enters the lung meridian, making it easy to disperse and descend and open the pores, thereby assisting Gegen (Puerariae Lobatae Radix) to dispel the pathogenic factors from muscles. Therefore, Gegen Qinlian Decoction is also sometimes used for exogenous fever with unexpected effects.

The most typical case is that Meizhong Yue once treated a child with epidemic encephalitis B.6 The child was 3 years old, male, admitted to the hospital with a high fever of 40°C, sweating, thirst, red face, dry lips, vomiting, yellow and moist tongue coating, bowel movement every 2 days with slightly loose stool, rapid pulse rate which was faster on the right than the left. At first, Meizhong Yue gave the pungent, cold heavy prescription Baihu Decoction. After 2 days of continuous use, high fever did not subside, bowel movements increased to four times every day, and symptoms of fright on hearing sound, rough breath, and vomiting and nausea were noticed, which means the disease tended to worsen. After thinking for a long time, Meizhong Yue realized that the child’s yellow and not dry tongue, vomiting and adverse flowing, and frequent diarrhea with loose stool resulted from the accumulation of summer heat and dampness in the spleen and stomach. The frequency of Renying pulse, red complexion, high fever, sweating, and slight panting of the patient indicated pathogenic factors on the surface. Therefore, original Gegen Qinlian Decoction was used. After administration of one dose, the fever was subdued to 39.4°C, and then to 38.8°C after taking two doses; bowel movement became better, and vomiting stopped. Soon, the patient recovered and was discharged from the hospital.

**For the Treatment of Hypertension and Diabetes**

In addition to the above applications, Gegen Qinlian Decoction has also been used for the treatment of hypertension and diabetes, which greatly expands its clinical application.
Zhiyuan Zhang, the national great master of Chinese medicine, has praised the hypotensive effect of Gegen Qinlian Decoction for many times, calling it the “secret formula of the Great Buddha’s Hall,” the natural enemy of hypertension, and roly-poly prescription. He believes that if this prescription is limited to sweating and panting due to misuse of the purgation method in cold damage, it will greatly restrict its application field. In fact, the hypotensive effect of this prescription can be explained in several perspectives, such as the pathogenesis, symptoms, and pharmacology.

First of all, from the point of view of the combination of the disease and syndromes, it is generally believed that liver yang transforming into wind is the basic pathogenesis of hypertension. However, the heart governs blood and pertains to wood. For high blood pressure due to excessive fire, the liver exuberant, the liver fire will be hyperactive, which will further lead to yang hyperactivity and stirring of wind. Therefore, clearing fire can calm yang and extinguish wind. In Gegen Qinlian Decoction, Huangqin (Scutellariae Radix), and Huanglian (Coptidis Rhizoma) are bitter in flavor and cold in nature, and they can clear visceral heat and enter the blood phase through clearing heat and purging fire. For example, Huangqin (Scutellariae Radix) was the single herb in Huangqin Powder in Taiping Holy Prescriptions for Universal Relief (Tai Ping Sheng Hui). In this case, the hypotensive effect of this prescription can be explained in several perspectives, such as the pathogenesis, symptoms, and pharmacology.

Secondly, at the symptom level, the main clinical manifestation of hypertension is dizziness. Gegen (Puerariae Lobatae Radix) is light in nature and functions to disperse. For the head and face diseases, the excess syndrome can be relieved by dispersing pathogenic factors, while the deficiency syndrome can be treated by lifting lucid yang to nourish the head. At the same time, Gegen (Puerariae Lobatae Radix) is also a special herb for the tightness and discomfort of the back and neck. Zhongjing Zhang also used Gegen (Puerariae Lobatae Radix) for those who were uncomfortable with the tightness of the back; for exterior deficiency, Guizhi Decoction plus Gegen (Puerariae Lobatae Radix) can be used; for the exterior excess syndrome, Mahuang (Ephedrae Herba) can be added; for patients with the tightness of the back and neck, Gegen (Puerariae Lobatae Radix) can be used. Hypertension is characterized by dizziness and tightness of the back and neck, which is obviously the advantage of Gegen (Puerariae Lobatae Radix) in therapeutic effects.

Third, Gegen (Puerariae Lobatae Radix) has a good blood-activating effect at the pharmacological level. This effect has been recognized since the Tang Dynasty. The Supplement to ‘The Grand Compendium of Materia Medica’ (Ben Cao Shi Yi) states that “The raw herb can break blood stasis, promote sore healing and induce abortion.” In the Rihuazi Herbal Medicine (Ri Hua Zi Ben Cao), it says Gegen (Puerariae Lobatae Radix) can: “expel pus and break blood stasis.” Modern pharmacological studies confirm that puerarin can inhibit platelet aggregation, prevent atherosclerosis, and reduce blood pressure; radices puerarire total flavone and puerarin can dilate coronary arteries and reduce myocardial oxygen consumption. At the same time, pharmacological studies have also demonstrated that Huangqin (Coptidis Rhizoma) can dilate vascular smooth muscle to achieve the antihypertensive effect. Therefore, Gegen Qinlian Decoction can be used for the treatment of hypertension with a combination of disease and syndrome differentiation. Zhiyuan Zhang believes that the antihypertensive effect of this prescription is no less than that of Xiaokucuo (Prunellae Spica), Gouteng (Uncariae Ramulus cum Uncis), Duzhong (Eucommiae Cortex), and more than that of Jue-mingzi (Cassiae Semen) and Sangjisheng (Taxilli Herba). It is suitable for headache and dizziness and head tightness like rope-binding. For those accompanied by dysphoria and bitterness in the mouth, stick stool, red tongue with yellow coating, rope-binding. For those accompanied by dysphoria and bitterness in the mouth, stick stool, red tongue with yellow coating, nausea, and anorexia, a relative large dosage of Shanzha (Crataei Fructus) can be used. It should be noted that it is not suitable for constipation patients since Gegen (Puerariae Lobatae Radix) functions to disperse and Huangqin (Scutellariae Radix) can dry the dampness and consolidate the intestine. If the stools change from sticky to dry during the administration, add some Dahuang (Rhei Radix et Rhizoma).

For the Gegen Qinlian Decoction in the treatment of diabetes, it is also comprehensively understood from the aspects of the disease, syndrome, symptoms, pharmacology, etc. Diabetes is mostly caused by unbalanced diet and internal heat impairing yin and consuming qi. Professor Qingguo Wang usually uses Gegen Qinlian Decoction as the basic prescription for the treatment. Professor Xiaolin Tong also believes that it is better
to combine nourishing yin with clearing heat than nourishing yin alone. In the prescription, Huangqin (Scutellariae Radix) and Huanglian (Coptidis Rhizoma) are bitter in taste, which can remove gastrointestinal heat accumulation, and Huanglian (Coptidis Rhizoma) has been proved to have an exact hypoglycemic effect. Gegen (Puerariae Lobatae Radix) is sweet in taste and cool in nature, which can stimulate the ascending of stomach qi and has the effect of promoting body fluid and quenching thirst. The classics of Shenmeng’s Classic of Materia Medica (Shen Nong Ben Cao Jing), Miscellaneous Records of Famous Physicians (Ming Yi Bie Lu) and Treatise on the Properties of Medicinals (Yao Xing Lun) have repeatedly stated that it can treat consumptive thirst. In recent years, pharmacological studies have proved that it has a hypoglycemic effect. Liangchun Zhu, a national great master of Chinese medicine, said that “for consumptive thirst, it is better to be treated by nourishing the lung and clear the heart at first, then nourishing the spleen and kidney, ascending primordial qi for long-term illness.” In clinical practice, Huangqi (Astragali Radix) is often used as the main herb, and Gegen (Puerariae Lobatae Radix) can be used to ascend primordial qi, assisted by Shanyao (Dioscoreae Rhizoma), Shanzhur (Corni Fructus), Zhimu (Anemarrhenae Rhizoma), and Huafen (Poll) to nourish the genuine yin so that yang get lifted and yin responded, which has a good effect. Jineijn (Galli Gigeriae Endothelium Cornueum) and Fuling (Poria) are used to assist the kidney and strengthen the spleen to generate body fluid. Wuweizi (Schisandrae Chinensis Fructus) and Shanzhur (Corni Fructus) are sour and astringent, which can be used to consolidate the kidney and prevent water retention from flowing downward. This is the key of herbal use for consumptive thirst.”

Professor Qingguo Wang believes that Gegen Qinlian Decoction is particularly suitable for early damp-heat internal resistance and yin impairment with clinical symptoms such as dry mouth and bitter taste in the mouth, thirst with desire for drinking, heartburn, red tongue and yellow coating, or with soft and rapid pulse; for patients with qi and yin deficiency in the advanced stage, Shengmai Drink can be combined or combines with Huangqi (Astragal Radix), Yuzhu (Polygonat Odorati Rhizoma), Tianhuafen (Trichosanthis Radix), etc.; for patients with severe liver and kidney yin deficiency, Liuwei Dihuang Pill can be combined; for patients with severe long-term qi stagnation and blood stasis, Sini Powder is often combined with Chuanxiong (Chuanxiong Rhizoma), Danshen (Salviae Miltiorrhizae Radix et Rhizoma), and Sanqi Powder to activate blood movement and dredge the collaterals.

Conclusion

Gegen Qinlian Decoction not only can clear away heat and dry dampness but also can descend the turbid and ascends the lucid. It can enter the meridians of stomach, large intestine as well as the heart and lung. It can also remove pathogenic factors from the interior and exterior, eliminate dampness and heat, and strengthen yin. In addition, it enters the Xuefen. With the combination of the four herbs, it can be used to treat a variety of digestive tract infections and noninfectious diseases, exogenous febrile diseases, and also hypertension and diabetes. The efficacy has been confirmed.

CRediT Authorship Contribution Statement


Funding

This work was supported by the Project of Traditional Chinese Medicine Academic School Inheritance Workshop Construction of the National Administration of Traditional Chinese Medicine - Yanjing Liu’s Typhoid Fever School Inheritance Workshop (LPGZS 2019-01), Project of Chinese Medicine Master Inheritance Workshop of National Administration of Traditional Chinese Medicine - Qingguo Wang Inheritance Workshop (2014011), and the Sixth Batch of National Chinese Medicine Senior Experts Academic Experience Inheritance Project of National Administration of Traditional Chinese Medicine (2017-01).

Conflict of Interest

The authors declare no conflict of interest.

References

3. Ma JX. Collations and annotations to Shenmeng’s Classic of Materia Medica (Shen Nong Ben Cao Jing). Beijing: People’s Medical Publishing House Co. Ltd; 2013;179, 156
11. Chen CQ, Collations and Explanations to Supplement to The Grand Compendium of Materia Medica (Ben Cao Shi Yi). Hefei: Anhui Science and Technology Press; 2004:42