Modulation of Gastrointestinal Bacterial in Chronic Atrophic Gastritis Model Rats by Chinese and West Medicine Intervention

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Abstract

Chronic atrophic gastritis (CAG) was well-known related with multiple pathogenic factors and normally therapies comprised by western or Chinese medicines. Present study was design to identified the bacterial community characterized by 16S rRNA amplicon sequencing and determine the modulate affection of bacterial composition response western and Chinese medicine Qing huayin (QHY) as well as antibiotic on model rats. Result shown the overall structure alteration of bacterial appeared under medicine applied, antibiotic caused a marked depletion in bacterial diversity and richness, the enrichment of *Firmicutes* (85.1-90.7%) in antibiotic-free convert to *Bacteroidetes* (30.7-34.6%) in antibiotic-added model rat were demonstrated. *Firmicutes* was most dominant phylum and accounting for 85.1%-90.5% and significantly decreased till 21.9%-68.5% in antibiotic-added treatments. Especially QHY-treated show highest RA of *Firmicutes* (90.5%) and the amelioration of CAG using QHY attributed by beneficial bacterial enrichment, especially *Ruminococcus*, *Lactobacillus* and *Bifidobacterium*. In addition, alpha and beta diversity analysis also demonstrated the clear dispersion and aggregation that revealed the alteration and steady of bacterial community structures. In summary, QHY has potential application value in the treatment of CAG which attributed to close relation with the modulatory of internal bacterial communities.

1. Introduction

Atrophic gastritis (AG) may be a chronic infection that primary structures are atrophy or and gastric organs intestinal metaplasia. As soon as, the oxyntic mucosa is included, atrophy primes to dearth of individually gastric acid and natural calculate generation in addition to iron or cobalamin malabsorption and in the long run anaemia. AG may be a complex condition which will emerge from long-standing *Helicobacter pylori* (Hp) contamination or within the setting of immune system gastritis (Lahner et al., 2018). To date, no universally acknowledged criteria are accessible to characterize immune system gastritis and to absolutely recognize this clinical entity from incessant, H. pylori-driven, multifocal atrophic gastritis (Rodriguez-Castro et al., 2018). Free epidemiological examination has affirmed that disease with *Hp* is the foremost imperative obtained aetiological mediator for gastric cancer, a worldwide driving basis of cancer associated deaths. The chronic inflammation initiated by *Hp* actuates a few histopathological variations within the gastric epithelium and keeps up a steady generation of a cascade of cytokines which in order to draws in resistant cells that create oxidative activists with the probable to harm host genetic materials. The instrument utilized by *Hp* in advancing the rise of pre-neoplastic gastric injuries (decay and intestinal metaplasia) is transcendentally chronic inflammation (Sung et al., 2020).

The stomach microbiota might moreover balance the concentrated and form of incendiary and safe reactions within the gastric mucosa. The microbiota investigation from stomach are rare and observed that the human stomach is inhabited via a multipart microbiota counting basically *Firmicutes*, *Proteobacteria*, *Actinobacteria* and *Fusobacterium* phyla and appeared clear differences with microbiota depicted within the mouth and esophagus (Aviles-Jimenez et al., 2014). TCM has been connected to the prevention and treatment of stomach related system issues in China for thousands of a long time (Yang
Chronic atrophic gastritis (CAG) may be a kind of the foremost common digestive system maladies in clinical practice, with assessed 50% of the world populace having the Hp contamination. And there's a need of compelling medicate for chronic atrophic gastritis (CAG) with around 20% repeat rate (Wei et al., 2015). Qinghuayin (QHY) is important Chinese formulation which is extensively utilized in the dealing of chronic atrophic gastritis (CAG) depend on the TCM models of defrayal heat and determining dampness. QHY is self-possessed of herbs, including Baibiandou, Fuling, Yiyiren, Yinchen, Peilan, Baidoukou, Huanglian, Houpu, and Chishao. A few Chinese investigation have described great effectiveness/protection of QHY in chronic atrophic gastritis (CAG) dealing. In other case, the fundamental components stay unclear (Li et al., 2018). On the other hand, extraordinary advance has been made in explaining the pathogenesis of CAG, most western solutions, counting Helicobacter pylori (Hp) eradication, corrosive concealment, and nonsteroidal anti-inflammatory drugs, stay unsatisfied. Due to chronicity and repeat of this illness, numerous sufferers have put their concentrations on elective medications such as conventional Chinese medicine (Dai et al., 2017).

The human gastro intestinal microbiota could be a multifaceted micro system, comprising roughly 1014 organisms from over 1,000 microbes, of which the phyla Bacteroidetes, Firmicutes and Actinobacteria account for over 90% of the species. In expansion, the hereditary variables, dietary propensities, and different natural components of the host initiate the differences and the specificity of the intestinal microbes, whereas intestinal flora would performed vital parts in applying host physiological capacities, for example digestion system, vitality ingestion, and safe control (Zhang et al., 2020). The intestine microbes are metabolized the TCM or co-metabolize TMC by means of host; the produced metabolites have shifting notches of bioavailability, bio-activity, and harmfulness. The configuration of the intestine microbiota for homeostasis recuperation can moreover be balanced usefully by TCM mechanisms. In this way, TCMs could enhance the dysfunction of the intestine microbiota in conjunction with significant neurotic environments (Lu et al., 2019).

Within the earlier period, the analysts was endeavored to uncover the helpful system of Chinese drugs by recognizing bio-compounds in Chinese medicines utilizing cutting edge science and innovation. In spite of much exertion, advance has been restricted. The standard worldview for medicate revelation from Chinese drugs includes herbal taking out, pre-fractionation, high throughput study directed via disease related targets (e.g., proteins, or RNA), testing models, and human trials. Utilizing such strategy, a few bio-compounds from Chinese medicine are undoubtedly established into present day drugs. Then, the trial rates could be exceptionally low. Many chemicals from Chinese medicines are demonstrated to be lacking or with small bio-action and bioavailability, and hence avoided from moreover dynamic substance of Chinese drugs or modern drug runners (Xu et al., 2017). Present study identified the bacterial community characterized by 16S rRNA amplicon sequencing to determine the modulate affection of bacterial composition response western and Chinese medicine Qing huayin (QHY) as well as antibiotic on model rats.

2. Materials And Methods
2.1. Preparation of test animals and medicinal

Fifty-nine male SPF Wistar rats with a body mass of \( (110 \pm 10 \text{ g}) \) were purchased from Shanghai Laboratory Animal Co., Ltd., and the animal permit license number was [SCXK(Shanghai) 2017-0005]. They were raised in SPF animal Experiment Center of Fujian University of Traditional Chinese Medicine in separate cages with ambient temperature of \( 23 \pm 2^\circ \text{C} \) and air humidity of \( 55 \pm 5\% \).

The traditional Chinese medicine "Qinghuayin" was prepared by the Pharmacy Department of the Second People's Hospital affiliated to Fujian University of Traditional Chinese Medicine. Medicine composition was composed by Atractylodes lancea (60 g), rhizoma coptidis (30 g), Magnolia officinalis Rehd. et Wils (60 g), Artemisia capillaris (100 g), Amomum cardamomum (30 g), Paeonia obovata Maxim (100 g), Agastache rugosa (90), Coix lacryma-jobi (200). The decoction process including boiled for three times (1.5, 1 and 0.5 hours respectively) after add eight times amount of water to soak for 0.5 hours. Then combine the decoction and filtrated, the filtrate was decompressed and concentrated to 500 ml at 60–70 \( ^\circ \text{C} \). Finally, the concentration of the solution was 1.34 g/mL containing crude medicine, sterilized and packed then stored in refrigerator at 4 \( ^\circ \text{C} \).

2.2. Grouping and model construction

SPF Wistar rats were divided into 2 groups randomly, one group of control was composed by 8 rats and fed with SPF standard diet. For modeling group, 51 rats were feed in the normal environment by drink freely with 120ug/ml 1-methyl-3-nitro-1-nitrosoguanidine solution, and gavage with 0.03 g/kg ranitidine daily and 45% ethanol twice a week on an empty stomach. At the same time, given feeding with starvation and satiety (fasting once a week, 24 hours for one time) for 24 consecutive weeks. After the above model building intervention, the modeled rats gradually appeared unkempt and loose fur with yellow and dull, squinted eyes, dull activities, arched back, huddled and decreased appetite. At the end of 24 weeks, 3 rats were randomly sacrificed, taken out stomachs and pathological examination was performed to determine the success of CAG model.

2.3. Medicine intervention, specimen preparation and collection

After the CAG model succeed construction, the modeled rats were divided into nine groups (each group has 8 rats) with control, model (normal saline), western vitaco-enzyme, traditional Chinese medicine, model (with antibiotic treatment), western vitacoenzyme (with antibiotic treatment) and Chinese medicine (with antibiotic treatment). According to the equivalent dose conversion of clinical application, the
traditional Chinese medicine group was gavage at the dose of the 5 ml/kg·d⁻¹ Qinghuayin, and the solution was diluted with normal saline to 5 ml each time according to the weight of the rats. The western medicine group were gavaged by suspension of vitacoenzyme with diluted 0.2 g/kg and 5 ml each time. In the antibiotic treatment group, Chinese and Western medicines were same as the above groups, but added antibiotic. The control and model group were given 5 ml of normal saline each time by gavage. The medicine intervention was constant 30 days.

After the corresponding medicine intervention, the rats were fasted for 12 hours and placed in transparent glass cover of a suitable size, then cotton ball soaked with ether was put into the glass cover to observe the breathing rhythm and movement situation of the rats. After successful anesthesia, the abdominal cavity was opened along the midline of the rat abdomen, and then separate the gastric and flush by normal saline, thereafter kept in frozen cryopreservation tube and quickly freeze in liquid nitrogen, finally stored in -80 °C for analysis.

2.4. Statistical analysis

Data shown are the means ± SD. T-test (prism 6.0) was used to analyze the data differences between the two groups. One way ANOVA (prism 6.0) was used to analyze the data difference more than two groups and the difference was significant (p < 0.05). The 16S rRNA microbial amplicon sequencing analysis was consistent with Zhang et al. (2015) and performed by Allwegene Technologies Co., Ltd.

3. Results And Discussion

3.1. Overall structural profile from phylum to genus in microbiota composition

In order to profile the specific distribution characteristics of the gastrointestinal microbial community in case of chronic atrophic gastritis (CAG) rats after medicine and antibiotic intervention, the relative abundance of the top taxa bacterial were identified from phylum to genes among all treatments (Fig. 1). At the phylum level, Firmicutes was most dominant phylum and accounting for 85.1%-90.5% in antibiotic-free treatments. Relatively higher relative abundance (RA) of Firmicutes were detected in medicine added group and QHY has richest abundance compare with control. The RA of Proteobacteria and Actinobacteria obviously increased in M and similar in other treatments. The RA of Bacteroidetes showed a certain level of reduction in medicine group compare with control (2.7–1.2%). While, distinct microbial distribution was described for antibiotic added treatments, the RA of Firmicutes was observed significantly decreased till 21.9%-68.5%. The RA of Proteobacteria showed a clearly increased with richest RA presented in M_ATB and V_ATB. Considerable enhance of Bacteroidetes richness was illustrated in QHY_ATB and V_ATB (37.7 and 30.7%).

At the class level, Clostridia was predominant in C, V, YHF M, QHY (45.6–71.7%), followed by Erysipelotrichia and richness in M and QHY, the RA of Bacilli was slightly increased in QHY and YHF (19.6 and 19.2%) than control (10.9%). On the contrary, Erysipelotrichia and Bacteroidia were dominant in
antibiotic treatments, the proportion of *Clostridia* significantly reduced (25.7–4.8%) and richest in M_ATB, the RA of *Erysipelotrichia* and *Bacteroidia* were sharply increased and richest in QHY_ATB and YHF_ATB. While the RA of *Bacilli* was decreased and similar abundance of *Gammaproteobacteria* and *Deltaproteobacteria* were increased compare with non-antibiotic treatments. At the order level, *Clostridiales* was dominant and richest in YHF, followed by *Lactobacillales* and relatively increased in medicine added treatments, *Erysipelotrichales* was richer in M and DHY. In contrast, antibiotic treatments were dominated by *Erysipelotrichales* and *Bacteroidales* that richness in QHY_ATB and YHF_ATB, while *Clostridiales* was dramatically reduced and the richness of *Enterbacteriales* and *Desulfovibrionales* were increased. At the family level, *Ruminococcaceae* (29.9–35.5%), *Lachnospiraceae* (20.8–26.1%) and *Lactobaciillaceae* (18.5–17.6%) were dominant in antibiotic-free treatments. While the RA of *Erysipelotrichaceae* was clearly increased in antibiotic treatments and richest in YHF_ATB and QHY_ATB. The proportion of *Enterobacteriaceae* and *Bacteroidaceae* were increased and *Lactobacteriaceae* was decreased (< 2%). When come to genus level, *unidentified* and *Lactobacillus* (11.7–18.5%) were dominant in non-antibiotic treatments. While antibiotic treatments were dominated by *Allobaculum* and *Bacteroides*, especially richness in YHF_ATB (33.5 and 26.9%) and QHY_ATB (55.7 and 33.1%), respectively.

Consistently, Fig. 2 shows the distribution alteration of dominant bacterial in each treatment, there is obvious aggregation effect in the transformation of different medicine intervention. In the case of apply antibiotic, the major proportion of bacterial from *Firmicutes* convert to *Firmicutes*, *Bacteroidetes* and *Proteobacteria* at phylum. Major class from *Clostridia* and *Bacilli* were convert to *Bacteroidia*, *Gammaproteobacteria* and *Erysipelotrichia*. For order, *Clostridiales* and *Lactobacillales* were convert to *Bacteroidales*, *Enterobacteriales* and *Erysipelotrichales*. While *Lachnospiraceae*, *Lactobacillaceae* and *Ruminococcaceae* convert to *Enterobacteriaceae*, *Bacteroidaceae* and *Erysipelotrichaceae* at family level. Superior genus from *Lactobacillus* and *unidentified* convert to *Bacteroides*, *Allobalulum* and *Escherichia-Shigella*, respectively.

Therefore, the heat map of bacterial RA altered by medicine and antibiotic treatment showed the significantly different distribution pattern of bacterial composition. *Firmicutes* and *Bacteroidetes* were two major phyla in rats and humans (Wei et al., 2018). The phylum of *Actinomycetes* were generally regarded as beneficial bacteria (e.g. *Bifidobacterium*) (Zareef et al., 2020). The phylum of *Bacteroides* including potential pathogen that could be disturb the immune function, and reduced in QHY treated rats that result revealed the inhabitation of potential pathogen. *Faecalibacterium* and *Roseburia* were involved butyrate generating, *Faecalibacterium* was known as functionally bacterial derived from salicylic acids and butyrate and anti-inflammatory molecule producing (Ou et al., 2019). *Lactobacilli* was considered and well-known as probiotic and the RA were significantly decreased in antibiotic feed model rats that would be impair intestinal metabolism, similar with Jaan et al. (2020) and Iino et al. (2018).

Chinese and western medicine-treated rats showed a slight difference in bacterial diversity while antibiotic caused a marked depletion in bacterial diversity and richness, which confirmed previous report (Fröhlich et al., 2016). However, analysis through all sequences detected, some distinct bacterial were
show increased patterns under reaction exposure on antibiotics in present study. Antibiotic group shown lower RA of beneficial bacteria while higher RA of pathogenic bacterial like Proteobacteria that same with Zhang et al. (2018). Rat in QHY has highest population of beneficial bacterial of Ruminococcus, Lactobacillus and Bacteroides, while decreased abundance of Desulfovibrio and Proteobacteria that suggesting QHY might be maintain the microbiota homeostasis.

3.2. Classification based comparison of phylum and genus levels

The abundance and evolutionary relationship of genus are visually displayed in phylogeny and cladogram (Fig. 3 and Fig. S1). The chiefly bacterial distributed in Firmicutes, Bacteroidetes and Proteobacteria that consist with Aggeletopoulou et al. (2019), while the composition of bacterial among distinct treatments presented a remarkably variations. To be specific, the dominant phylum of Firmicutes was richness with Ruminococcaceae, Peptostreptococcaceae, Lachnospiraceae, Clostridiaceae_1, Lactobacillaceae and Staphylococcaceae. The Bacteroidetes was richen in Bacteroidaceae and Prevotellaceae. The Proteobacteria was mainly distributed by Enterobacteriaceae, Desulfovibrionaceae, Helicobacteraceae, Alcaligenaceae and Campylobacterales. The phylum of Actinobacteria was distributed by Coriobacteriaceae. The Cyanobacteria was occupied by Veillonellaceae and Gastranaerophilales. It can be observed that the distribution of the bacterial from distinct treatments were different through discriminant transformation effect. Among the superior microbiome phylotypes modulated by Chinese medicine and antibiotic in rats, we observed several putative beneficial genera containing Lactobacillus, Paraprevotella and Eubacterium. A pronounced depletion of Clostridiales and recovery of Bacteroidales were detected in antibiotic treatments, the RA of Enterobacteriales and Verrucomicrobiales were boosted at antibiotic treatment. Rats with antibiotic has obviously higher abundance of Bacteroides and lower Clostridium that may palliation the opportunities for pathogenic infection (Zhang et al., 2015ab; Lv et al., 2017).

The remarkably proportion of Lactobacillus in medicine group than antibiotic treated rats that might be related with the protective effect of Chinese medicine. Chinese medicine has been considered as an important therapy to ameliorate adverse antibiotic reaction comprised diarrhea and dysbiosis (Jaan et al., 2020). The main way for Chinese medicine to promote the proliferation of gut microbial is to play key role of prebiotic-like and selectively stimulating the metabolism of symbiotic beneficial bacterial, such as Lactobacillus, Bacteroides and Bifidobacterium (Xu et al., 2017). Various member of Lactobacillus has beneficial or positive effect on colitis and gastroenteritis model test (Rodríguez-Nogales et al., 2017; Chang et al., 2017; Szajewska et al., 2019). In addition to having beneficial effects on host physiology, some component of symbiotic bacterial could be secrete molecules to limit microbial metabolism and proliferation (Suez et al., 2018). Turroni et al. (2014) found the alteration of Lactobacillales and Bifidobacteriales might be related to microbiota components owing to enable to suppress the metabolic and proliferation of microbiota through decreasing the number or diversity of observed genus and regulate microbial community structure (Suez et al., 2018). Present finding obviously illustrated the intestinal biotransformation of CAG was observably strengthened by Chinese medicine.
3.3. Diversity analysis based on alpha and beta

In order to comprehensively identify the changes in the composition of the intestinal bacterial of CAG rat after interventions with normal saline, Chinese and western medicines as well as antibiotics, alpha and beta diversity analysis were performed to determine whether the community structure and steady state have changed (evaluated from the perspective of diversity and uniformity). The bacterial richness index based on the number of OTUs in the bacterial community was present in Chao1 (Fig. 4a), 1092, 865, 854, 1005, 994, 146, 157, 122 and 84 were detected in C, M, QHY, V, YHF, V_ATB, M_ATB, QHY_ATB and YHF_ATB, respectively. The actually number of OTUs observed with the increase of sequencing depth was shown in observed_species (Fig. 4b), 795, 627, 626, 804, 797, 88, 101, 72, and 57 were identified in the above treatments, respectively. The pedigree diversity based bacterial abundance and evolutionary distance were performed in PD_whole_tree (Fig. 4c). The result shown 58, 46, 45, 51, 54, 13, 12, 9 and 8 were discovered in C, M, QHY, V, YHF, V_ATB, M_ATB, QHY_ATB and YHF_ATB, respectively. As well as Shannon (Fig. 4d) demonstrated 6, 5, 5, 6, 3, 3, 3 and 2 were present in above treatments, respectively. Therefore, bacterial diversity of antibiotic apply treatments were obviously decreased. The Venn figure also verified the same results (Fig. S2) that indicated the metabolism conspicuously weakened by antibiotic intervention.

The beta diversity aspect of principal component (Fig. 5a) and non-metric multi-dimensional scaling analysis (Fig. 5b) were carried out to compare the bacterial community structures, further demonstrated an obviously separation among different treatments of overall bacterial structure in rat after Chinese medicine and antibiotics treated. The principal components were account for 60.27% and 10.57% of the total variation respectively. Treatments of C, YHF and V were clustered one group, M and QHY gathered together, V_ATB and M_ATB distributed one group, QHY_ATB and YHF_ATB gather together and have intersection. In addition, weighted (Fig. 5c) and unweighted_unifrac (Fig. 5d) also demonstrated the difference among treatments. The degree of dispersion between the medicine added and the antibiotic group were different significantly. The west and Chinese medicine group has an overlap and large dispersion with antibiotic group. The affection of antibiotics is mainly focus on reduce the diversity and richness of beneficial intestinal microorganisms, aggravate the intestinal microbial imbalance and increase the probability of the intestinal pathogen invasion and attachment, further caused more serious damage to the intestinal barrier function (Brugiroux et al., 2016). The diversity of gastrointestinal microbial composition enables to resist the adverse altered in the environment and recover equilibrium after perturbation (resistance and resilience) (Jaan et al., 2020), which was positively facilitated by Chinese medicine.

3.4. Correlation analysis among superior genus based on network

The niche-specific microbial network can be reflected the disease microenvironment. Coker et al. (2017) observed the co-occurrence and co-exclusion interaction between GC enrichment and replacement bacteria were increasing with disease progression. Disease-related bacterial can interact and build a
synergistic network that may contributions to the diseases. To be specific, present study was presented intricate correlations among richness genus, \textit{Lactobacillus} was strongly positive with \textit{Ruminococcaceae\_UCG\_005} and \textit{Christensenellaceae\_R7}, negative with \textit{Subdoligranulum}, \textit{Klebsiella} and \textit{Lachnoclostridium}. The bacterial of \textit{Bacteroides} was positively with \textit{Klebsiella}, \textit{Akkermansia} and \textit{Subdoligranulum}, negative with \textit{Eubacterium\_coprostanoligenes} and \textit{Lachnospiraceae\_NK4A136}. The genus of \textit{Bilophila} with \textit{Subdoligranulum}, \textit{Akkermansia} and \textit{Eubacterium\_nodatum} shown a strong negative correlation. In addition, genus of \textit{Blautia} was positively correlated with \textit{Ruminococcaceae\_UCG\_014}, \textit{Ruminococcaceae\_NK4A214}, \textit{Lachnospiraceae\_NK4A136} and \textit{Eubacterium\_coprostanoligenes}, negative with \textit{Klebsiella}, \textit{Akkermansia} and \textit{Subdoligranulum}. \textit{Akkermansia} was positive related with \textit{Bilophila}, \textit{Subdoligranulum}, \textit{Morganella}, negative related with \textit{Ruminococcaceae} and \textit{Lachnospiraceae}\ (Fig. 6).

In view of \textit{Blautia} can be convert carbohydrates and proteins to acetic acid and further responsible for energy supply. While many researches demonstrated the RA of \textit{Blautia} was increased in diseases condition such as diabetes, irritable bowel syndrome due to it can be activate inflammatory cytokines (Yan et al., 2016), which was same with present study and the RA was obviously increased in M-treated. \textit{Clostridium} is the main bacteria producing butyric acid and further fermentation convert to short-chain fatty acids that play an important role in maintaining host health and disease prevention. It can provide the host colonic epithelial cells and promote the growth of intestinal epithelial cells, accelerate the repair of damaged intestinal mucosa, also physiologically regulate the gene expression of intestinal epithelial cells that effectively inhibit the occurrence of enteritis and colorectal cancer. \textit{Akkermansia} as a mucus-degrading bacterial that exists in the mucus layer (Everard et al., 2013), which enhance the integrity of the intestinal barrier and regulate intestinal metabolism (Ottman et al., 2017).

Interestingly, Chinese medicine intervention restored the microbial community perturbed by CAG holistically that consistent with Zhou et al. (2016) and the mechanisms involved can be intricate. After the intervention of antibiotics, the specific bacterial such as \textit{Enterococcus}\ \textit{spp.} multiplies that is related to the survival requirement and colonization mechanism of the organism (Manuelf et al., 2014). When long-term use of antibiotics might be caused gastrointestinal diseases, pathogens such as \textit{Escherichia coli} will proliferate while probiotics like \textit{Bifidobacterium}, \textit{Lactobacillus}, \textit{Bacteroides} were reduced significantly, showing a state of intestinal microecosystem disorders. At the same time, the imbalance of microbial will in turn affect the absorption of nutrients, reduce the immunity, weaken the intestinal barrier function, and further aggravate the disease. The genus of \textit{Enterococcus} can produce tyramine that was related to tyrosine metabolism and can enhance the adhesion of bacteria to the intestinal, further improving colonic mucosal adhesion (Jaan et al., 2020). The RA of \textit{Desulfovibrio} and \textit{Bilophila} were increased that indicated the selective specific bacterial community correlated with inflammation has altered in case of antibiotic application (Tang et al., 2018).

The mechanism of Chinese medicine action on the weakened spleen and stomach CAG was mainly to protect the gastric mucosa and reduce inflammation, improve gastric mucosal secretion and regulate gastrointestinal motility, the curative effect is accurate and the safety is high. Zhou et al. (2016) also
verified Chinese medicine ginseng stimulated the growth of crucial probiotics *Lactobacillus* and *Bacteroides*. The increase in the number of beneficial bacteria in the intestines *Lactobacillus* is of great significance for inhibiting the proliferation of spoilage bacteria and enhancing the immunity and resistance of the body. This study suggests that the total number of bacteria and *Lactobacillus* during the treatment of QHY have shown a growth trend, chronic atrophic gastritis disrupts the balance of the normal microbial community, the application of Chinese medicine can recover new balance and more optimized by improving the structure of the intestinal microbial diversity, while its metabolic pathway of action needs further study.

### 4. Conclusion

The gastrointestinal bacterial composition was obviously different of the CAG model group under the medicine intervention. Antibiotic treated model rats remarkably decreased the richness and diversity of bacterial community, prevent the depletion of *Firmicutes* (85.1%-20.3%) and expanded the *Bacteroides* (37.7% in QHY_ATB). Chinese medicine QHY prominently ameliorated GCA induced gastrointestinal injury by promoting effect on the proliferation of *Lactobacillus* (11.7–18.5%), which effect on protection of the gastric mucosa barrier and beneficial regulation of the microbial, while its metabolic pathway of action needs further study.

### Declarations

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