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Review of Relationship of Chinese Cream Formula, Water-Soluble Dietary Fiber and Intestinal Microflora Regulation

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Abstract

Water-soluble dietary fibers stimulate the proliferation of probiotics by selectively stimulating the growth of probiotics. At the same time, it inhibits the growth and reproduction of exogenous and innate enteral spoilage bacteria and forms a microecological competitive advantage, which is beneficial for normal intestinal bacteria to play the function in shielding, nutrition and immunity, and improve the intestinal microflora. Now we can supplement the body´s soluble dietary fiber through Chinese cream formula, which can become a new direction of regulating human intestinal flora and daily health care.

Key words: Cream formula; Water-soluble dietary fiber; Intestinal microflora; Cream formula process

The study of human microorganism group with the intestinal microflora as the core has become a hot topic in the international mainstream biomedicine. The microecological balance of human intestinal flora (including probiotics beneficial to the human body and potential deadly bacteria) is closely related to health. However, as people age, the probiotics of human intestinal tract will gradually decrease. If the living probiotics are directly implanted into the human body to supplement the probiotics, no obvious effect could be achieved because the preservation of probiotics living preparation is poor. At present, applying a material that can promote probiotics proliferation to improve probiotics in the body will be a more acceptable routine [1-2]. Therefore, this paper made a constructive discussion on the regulation of water soluble dietary fiber on human intestinal microflora and the traditional cream formula and balance signal transduction of microbial flora in modern times.

Cream formula, one of the eight types of traditional Chinese medicine preparation, is a kind of semifluid thick preparation, which has a complicated process: decocting herbs with water repeatedly, removing the dregs, then concentrating the decoction with evaporation, and finally mixing the decoction with colloidal drugs and honey. Cream formula, with a long history of application,has been highly praised by many doctors in the past . As one of the special therapies of Chinese medicine, it is often used to nourish and strengthen the body, maintain zang-fu organs, dispel pathogenic factors, eliminate ailments, etc. Historically, cream formula was the superior tonic for rich and high-born families. In the last two decades, as the improvement of the living standard of people, cream formula has become the first choice of "tonifying in winter" with the increasing favor, which has made its usage reached the peak of history. Thus, how to guide the scientific development of cream formula and how to prevent its blind application have become one of the hottest issues in the medical community and society. To promote the scientific development of the cream formula researches, to guide the optimization of cream formula's drug selection, preparation, administration and treatment, and to make Chinese medicine better serve the public's health, it is necessary for us to analyze and summarize drug selection characteristics, efficacy components, main efficacy, indications and usage of the cream formula.

1 Drug Selection Characteristics of Cream Formula

Herbs chosen for cream formula should be with a large amount of cream. Most herbs are food and drug resources, and a few herbs are grasses, leaves and minerals with bitter taste and cold nature or higher starch content.

1.1 *Main Herbs with a large amount of cream are:*

1. Chinese Medicine of Rhizoma: ren shen (*Radix Ginseng*), huang qi (*Radix Astragalus*), dang shen (*Radix Codonopsis*), bai zhu (*Rhizoma Atractylodis Macrocephalae*), shan yao (*Rhizoma Dioscoreae*), gan cao (*Radix et Rhizoma Glycyrrhizae*), dang gui (*Radix Angelicae Sinensis*), shu di (*Radix Rehmanniae Praeparata*), bai

shao (*Radix Paeoniae Alba*), he shou wu (*Radix Polygoni Multiflori*), gu sui bu (*Rhizoma Drynariae*), xu duan (*Radix Dipsaci*), nan sha shen (*Radix Adenophorae*), bei sha shen (*Radix Glehniae*), mai dong (*Radix Ophiopogonis*), tian dong (*Radix Asparagi*), yu zhu (*Rhizoma Polygonati Odorati*), huang jing (*Rhizoma Polygonati*), xi yang shen (*American ginseng*), xuan shen (*Radix Scrophulariae*), hong jing tian (*Radix et Rhizoma Rhodiolae Crenulatae*), chai hu (*Radix Bupleuri*), tian ma (*Rhizoma Gastrodiae*), zi yuan (*Aster*), bai bu (*Radix Stemonae*), yu jin (*Radix Curcumae*), tai zi shen (*Radix Pseudostellariae*), ge gen (*Radix Puerariae Lobatae*), chuan xiong (*Rhizoma Chuanxiong*), ze xie (*Rhizoma Alismatis*), huai niu xi (*Achyranthes Bidentata*), bai ji (*Rhizoma Bletillae*), mu xiang (*Radix Aucklandiae*), bai he (*Bulbus Lilii*), jie geng (*Radix Platycodonis*).

2. Chinese medicine of Fruits and Seeds: long yan rou (*Arillus Longan*), da zao (*Fructus Jujubae*), qian shi (*Semen Euryales*), lian zi (*Semen Nelumbinis*), yi yi ren (*Semen Coicis*), bai guo (*Semen Ginkgo*), yi zhi ren (*Fructus Alpiniae Oxyphyllae*), tu si zi (*Semen Cuscutae*), sha yuan zi (*Semen Astragali Complanati*), gou qi (*Fructus Lycii*), shan zhu yu (*Fructus Corni*), nv zhen zi (*Fructus Ligustri Lucidi*), bai zi ren (*Semen Platycladi*), sang shen (*Mulberry*), hei zhi ma (*Semen Sesami Nigrum*), bai bian dou (*White Hyacinth Bean*), wu wei zi (*Fructus Schisandrae Chinensis*), raisin, yin er (*Tremella*), shan zha (*Fructus Crataegi*), che qian zi (*Semen Plantaginis*), he tao ren (*Semen Juglandis*), mai ya (*Fructus Hordei Germinatus*), gu ya (*Fructus Setariae Germinatus*), zao ren (*Semen Ziziphi Spinosae*), yu li ren (*Semen Pruni*), xing ren (*Semen Armeniacae Amarum*), tao ren (*Semen Persicae*), luo han guo (*Fructus Momordicae*), chen pi (*Pericarpium Citri Reticulatae*), fo shou (*Fructus Citri Sarcodactylis*) and zhi qiao (*Fructus Aurantii*).

3. Chinese Medicine of animals: gui ban (*Plastrum Testudinis*), bie jia (*Carapax Trionycis*).

4. Chinese Medicine of Whole Grasses: shi hu (*Caulis Dendrobii*), rou cong rong (*Herba Cistanches*), suo yang (*Herba Cynomorii*), sang ji sheng (*Herba Taxilli*).

5. Chinese medicine of stem bark: hou po (*Cortex Magnoliae Officinalis*), dan pi (*Cortex Moutan*), du zhong (*Cortex Eucommiae*), ba ji tian (*Radix Morindae Officinalis*).

6. Colloidal Chinese medicine: e jiao (*Colla Corii Asini*), lu jiao (*Colla Cornus Cervi*), gui jiao (*Colla Testudinis Plastri*).

7. Chinese medicine of phycomycete and others: jun ling zhi (*Ganoderma*), zhu ling (*Polyporus)*, fu ling (*Poria*), shen qu (*Massa Medicata Fermentata*), etc.

Most herbs used for cream formula are food and drug resources. And herbs containing polysaccharides that is soluble dietary fiber, are not used.

1.2 *Colloidal drugs from animals are often used in cream formula*

During the process of cream preparation, if colloidal content from animals (e.g. e jiao (*Colla Corii Asini*), gui ban jiao (*Colla Testudinis Plastri*)) or animal drugs (e.g. placenta, penis cervi) are added, the product is called animal cream, otherwise it is called plain cream.

Colloidal drugs from animals are rich in gelatin that is equal to gelatin enteric capsule, which can reduce the active ingredients of gastric acid destruction.

1.3 *Honey is often used in cream formula*

During the preparation, when the decoction has been completely thickened without adding sugars and colloidal drugs, the cream formula is called clear cream. And the thick cream that is mixed with sugars (e.g. honey, crystal sugar, brown sugar, maltose) is called honeyed cream (also called "soft extract"). The purpose of adding sugars is to make the cream taste better. In addition, it also can strengthen the middle-energizer and relax tension.

The raw honey is rich in a variety of natural strains and spores, which is aimed to increase the diversity of intestinal microflora.

1.4 *The cream formula is thick and dense*

Elucidations of Script and Explications of Characters explains that "gao refers to cream or grease", which means that "gao" is a kind of thick paste with coagulating but not hard property. It often refers to the essence of things, thus it has the effect of nourishing, harmonizing and moistening.

With dense nature, the cream formula is isolated from oxygen, which can prevent the denaturation of active peptides and enzymes, and inactivations of strains during long term storage.

2. The main component of cream formula

Herbs with a large amount of cream are chosen for cream formula. During the processing, the decoction is remained and the dregs (insoluble fibers, such as cellulose, lignin, etc.) are removed. Thus, in addition to protein, fat, monosaccharide, disaccharide and oligosaccharide, the cream formula is also rich in water-soluble fiber.

2.1 *The cream formula is rich in water-soluble dietary fiber and water-soluble non-starch polysaccharides (NSP)*

2.1.1 Herbs are rich in water-soluble dietary fiber

Generally, herbs with plenty of pectin, plant gum and viscose are rich in water-soluble NSP. This kind of herbs include yu zhu (*Rhizoma Polygonati Odorati*), huang jing (*Rhizoma Polygonati*), mai dong (*Radix Ophiopogonis*), tian dong (*Radix Asparagi*), ren shen (*Radix Ginseng*), dang shen (*Radix Codonopsis*), huang qi (*Radix Astragalus*), bai zhu (*Rhizoma Atractylodis Macrocephalae*), shan yao (*Rhizoma Dioscoreae*), gan cao (*Radix et Rhizoma Glycyrrhizae*), dang gui (*Radix Angelicae Sinensis*), shu di (*Radix Rehmanniae Praeparata*), bai ji (*Rhizoma Bletillae*), zhi mu (*Rhizoma Anemarrhenae*), gu sui bu (*Rhizoma Drynariae*), nan sha shen (*Radix Adenophorae*), bei sha shen (*Radix Glehniae*), hong jing tian (*Radix*

et Rhizoma Rhodiolae Crenulatae), tian ma (*Rhizoma Gastrodiae*), tai zi shen (*Radix Pseudostellariae*), bai he (*Bulbus Lilii*), long yan rou (*Arillus Longan*), da zao (*Fructus Jujubae*), tu si zi (*Semen Cuscutae*), gou qi (*Fructus Lycii*), shan zhu yu (*Fructus Corni*), sang shen (*Mulberry*), hei zhi ma (*Semen Sesami Nigrum*), bai bian dou (*Semen Lablab Album*), wu wei zi (*Fructus Schisandrae Chinensis*), raisin, yin er (*Tremella*), ting li zi (*Semen Descurainiae*), che qian zi (*Semen Plantaginis*), ya ma zi (*Semen Lini*), he tao ren (*Semen Juglandis*), mai ya (*Fructus Hordei Germinatus*), gu ya (*Fructus Setariae Germinatus*), zao ren (*Semen Ziziphi Spinosae*), yu li ren (*Semen Pruni*), xing ren (*Semen Armeniacae Amarum*), tao ren (*Semen Persicae*), luo han guo (*Fructus Momordicae*), chen pi (*Pericarpium Citri Reticulatae*), fo shou (*Fructus Citri Sarcodactylis*), zhi qiao (*Fructus Aurantii*), shi hu (*Caulis Dendrobii*), rou cong rong (*Herba Cistanches*), sang ji sheng (*Herba Taxilli*), du zhong (*Cortex Eucommiae*), jun ling zhi (*Ganoderma*), zhu ling (*Polyporus*), fu ling (*Poria*) and kun bu (*Thallus Eckloniae*), etc.

The content of dietary fiber in dried lily bulb accounts for 20.3%. Generally, the water content of yam is 75%.

2.1.2 Fruits and vegetables are rich in water-soluble dietary fiber

Generally, fruits and vegetables with plenty of pectin, plant gum and viscose are rich in water-soluble NSP. This kind of fruits and vegetables include citrus, lemon, banana, apple pomegranate, edible fungi, sea-tangle, laver, konjak, chicory, jerusalem artichoke, Chinese artichoke, lycopus lucidus, lotus root, beans, tomatoes, onion, carrot, day-lily, malabar spinach, okra and aloe, etc.

2.2 *The similarities and differences of water-soluble dietary fiber and water-soluble NSP*

2.2.1 Water-soluble dietary fiber in dietary fiber

Dietary fiber can be defined from two aspects: Physiologically, it is defined as the remnants of plant cells in the mammalian digestive system that are not digested directly by self-secreted enzymes, including cellulose, hemicellulose, pectin, gum, resistant starch and lignin, etc. Chemically, dietary fiber is defined as NSP and lignin in plants. Dietary fiber can be divided into two categories: water-soluble dietary fiber and insoluble dietary fiber.

Insoluble dietary fiber refers to a type of fiber that is unsolvable in water and unhydrolysable by microorganisms in the large intestine, which is often found in roots, stems, trunk, leaves, skins and fruits of plants. It mainly includes cellulose, lignin and some hemicellulose, etc.

Soluble dietary fiber refers to a type of fiber that is solvable and swellable in water, and hydrolysable by microorganisms in the large intestine, which is often found in cell fluid and intercellular substance of plants. It mainly includes pectin, plant gum, viscose and some hemicellulose that originate pectin, phycocolloid and konjak, etc.

2.2.2 Water-soluble NSP

Polysaccharide is a polysaccharide chain containing over 10 saccharide grous that composed of many monosaccharide molecules linked by glycosides. Because of different linking ways, it can form straight chain polysaccharides, fork chain polysaccharides, and cyclic polysaccharides.

NSP are polymers of various monosaccharides and aluronic acids linked by glycosidic bonds in plant tissues. Most NSP are branched chain structures, and often bind to inorganic ions and proteins. NSP is the essential component of cell wall, which is difficult to be hydrolyzed by self-secreted digestive enzyme of monogastric animals. NSP are generally classified into three main categories, namely cellulose, non-fibrous polysaccharides (hemicellulose polymer) and pectin. Among them, non-fiber polysaccharides also include xylan, β-glucan, mannan, galactan, etc. According to the component unit, NSP can be divided into homopolysaccharide and heteropolysaccharide. Homopolysaccharide mainly includes cellulose, β-glucan, araban and mannan. Heteropolysaccharide mainly includes araboxylan, galactan, glucan and pectin class.

According to water-solubility, NSP can be divided into water-soluble NSP (SNSP) and insoluble NSP (INSP). INSP mainly includes cellulose, pentosan and pectic polysaccharides, etc. SNSP mainly includes araboxylan, β-glucan, mannan and pectin, etc.

2.2.3 The tests of water-soluble dietary fiber and water-soluble NSP

Enzymes-weight method of Prosky can test total dietary fiber (TDF), insoluble dietary fiber (IDF) and water-soluble dietary fiber (SDF), but it can't detect the specific polysaccharides among the measured fibers. Enzyme-chemistry assay of Theander tests the obtained fibers after decomposing them into various monosaccharides, in which SNSP, INSP and lignin can be determined. This method can determine the type of fiber polysaccharides, thus it can represent the actual fiber content.

2.2.4 The differences between water-soluble dietary fiber and water-soluble NSP

The differences between water-soluble dietary fiber and water-soluble NSP are as follows: Water soluble dietary fiber includes NSP and oligose (oligose is also called oligosaccharides: a sugar molecule composing 2-10 monosaccharide units linked by glucoside bond)..Generally, after the herbs are boiling, partial water-soluble NSP will degrade into oligosaccharides. Thus, the cream formula is rich in water-soluble dietary fiber because the herbs are rich in water-soluble NSP.

3 Primary effect of water-soluble dietary fiber

The key pharmacological effect of cream formula depends on the water-soluble dietary fiber in it.

3.1 *Primary functions of water-soluble dietary fiber*

3.1.1 preventing and treating constipation

After being fermented by bacteria in the large intestine, dietary fiber has strong abilities of absorbing or combining with water, which can soften the feces in the intestines and have laxative effect. Meanwhile, with large volume, dietary fiber can promote intestinal peristalsis, reduce food retention time in the stomach and intestines, which makes its moisture content is not easily absorbed.

3.1.2 Preventing carcinoma of colon and rectum [3-6]

Carcinoma of colon and rectum are mainly caused by long-term exposure of carcinogens to the intestinal wall. The increase of dietary fiber intakes can decrease the concentration of carcinogens, while dietary fiber can stimulate peristalsis and shorten the contact time between harmful substances and intestinal wall.

3.1.3 Reducing blood fat and preventing coronary heart disease [3-6]

Dietary fiber can combine with cholic acid and cholesterol, so that it can be discharged directly from the feces. Therefore, the consumed cholesterol in the body can supplement that consumed in the bile, which reduces the cholesterol and prevents the coronary heart disease.

3.1.4 Preventing and treating diabetes [3-6]

The pectin in the dietary fiber can prolong the retention time of food in the intestines, reduce the rate of glucose entering the intestinal mucosa cells, control the degradation effect of amylase on starch and restrain glucose by adsorptive enzyme, reduce the effective concentration of glucose in the intestinal fluid, make the blood glucose not rise sharply after meal. So pectin in the dietary fiber can be a benefit for people with diabetes. In addition, the long-term increase of dietary fiber in patients' diet can improve the sensitivity of insulin receptor, reduce the insulin requirement and control the metabolism after meal, which can be used as a supplementary therapy for the treatment of diabetes.

3.1.5 Bacterial fermentation effect

In the intestinal tract, dietary fiber is easily leavened by bacteria, among which the soluble fiber can be completely leavened by bacteria, while insoluble dietary fiber is not easily leavened. The produced short-chain fatty acid after fermentation, such as ethyl acetate acid, propyl acid and butyl ester acid, can be used as energy sources for intestinal cells and bacteria.

3.2 *Water-soluble dietary fiber improves intestinal microflora by increasing beneficial bacteria*

Due to the lack of digestive enzymes of water-soluble fiber in human digestive tract, the ingested water-soluble fiber can directly enter the intestine. In the large intestine, water-soluble dietary fiber can be degraded by extracellular glycosidase that is secreted by probiotics, then is absorbed and utilized. In this way, water-soluble dietary fiber can selectively stimulate the growth of probiotics, make them full of vitality, and enrich the beneficial strains. In addition to being the carbon source of probiotics, water-soluble dietary fiber can also serve as a substrate for probiotics fermentation. Water-soluble dietary fiber can produce short-chain fatty acids, meanwhile, bifidobacteria and Lactobacillus acidophilus also produce lactic acid in their metabolism, which can reduce intestinal PH. Moreover, the acidic environment has bacteriostatic and bactericidal effects, which can competitively inhibit the growth and reproduction of acid-intolerant bacteria in the intestine. Water-soluble dietary fiber promotes the proliferation of probiotics and inhibits the growth and reproduction of exogenous and enteral spoilage bacteria, which forms the competitive advantage of microecology. Thus, it is beneficial for the normal enteric bacteria playing roles in prevention, nutrition and immunity, which improves the intestinal microflora. It is a good probiotic proliferation factor [7].

3.2.1 Daily intake standard of dietary fiber

WHO and national nutrition circles in various countries give a unified suggestion on dietary fiber intake: The daily intake of each person should be 25-35 g. Among them, the American Diabetes Association recommends that the intake of patients with diabetes can moderately increase to 45-55 g. The world Food and Agricultural Organization (FAO) recommends a daily intake of 2 g/person for the normal population. European Community Food Science Committee recommends a standard daily intake of 30 g/person. American Cancer Society (ACS) recommends a standard daily intake of 30-40 g/person. In 2000, the Dietary Nutrients Intakes Reference for Chinese Residents newly released by China Nutrition Institute suggests that the daily dietary fiber intake should be 25-35 g [8]. The quantity and range of food dietary fiber: low-calorie diet wth1 800 kcal needs 25 g/d intake; medium-calorie diet with 2 400 kcal needs 30g/d intake; high-calorie diet with 2 800 kcal needs 35 g/d intake. In daily dietary fiber intake, the proportion of insoluble fiber and water-soluble fiber should be appropriate. For example, insoluble fiber 20 g and water-soluble fiber 10 g are suitable.

3.2.2 Chinese residents' dietary fiber intake is insufficient

White Paper of Dietary Fiber Intake for Chinese Residents indicates that the dietary fiber intake of Chinese residents is generally insufficient with a downward trend. At present, the intake of insoluble dietary fiber per capita is 11 g/d, and the urban situation is basically in line with that of the rural areas. Due to the lack of soluble dietary fiber data in food composition table, the estimated total dietary fiber is about 13 g/d with conversion coefficient. Comparing with the recommended dietary fiber intake in Dietary Nutrients Intakes Reference for Chinese Residents, population that can achieve 25 g/d intake is less than 5%. Usually, insoluble dietary fiber intake can be sufficiently supplemented by grain, coarse grain, vegetables and fruits of daily diets, but the soluble dietary fiber intake is often inadequate. On the basis of recommended daily dietary fiber in-

take, apart from daily consumption of grain (50-100 g), vegetables (300-500 g) and fruits (200-400 g), Chines people also need to be supplemented the deficient water-soluble dietary fiber.

3.2.3 Supplementing water-soluble dietary fiber in human body by cream formula

From the view of historical development, cream formula is mainly used for "clearing and tonifying spleen and stomach", and "preventing diseases". The Complete Compendium of Cream Formula of Bowei Qin records that "Cream formula refers to the thick fluid that decocted by herbal juice. Because it can be used for nourishing and moistening the dryness, deficiency and weakness of five-zang organs and six-fu organs, thus it is commonly called jelly drug". The cream formula can embody the characteristic of "preventing diseases" and the advantages of Chinese medicine. It can be applied to various population and improve the constitution bias. For healthy people, it can prevent the risk of "getting ill"; for sub-healthy population, it can prevent the risk of "disease formation"; for high-risk population, it can prevent the risk of "morbidity"; for diseased people, it can prevent "transmission of disease", and for rehabilitative population, it can prevent the "reoccurrence of the disease".

The essence of cream formula lies in the richness of water-soluble dietary fiber. Water-soluble fiber is solvable and swellable in water so its volume and weight can be increased by 10-15 times, which can increase satiety, reduce the absorption of fat and sugar in food, reduce the heat ratio of fat in food, relatively control and decrease food total calories, avoid excessive accumulation of fat in the body induced by excess heat energy. For population with obesity, hyperlipidemia, hypercholesterolemia and fatty liver, water-soluble fiber has a positive effect. Water soluble dietary fiber has the best effect in controlling rapid increase of postprandial blood glucose and improving glucose tolerance. Water-soluble dietary fiber is a kind of food for intestinal probiotics. Adequate intake of water-soluble dietary fiber can promote the proliferation of intestinal probiotics. If the water-soluble dietary fiber intake is insufficient, the probiotics will not be able to survive and reproduce, and can't create good intestinal conditions. Although vegetables such as sea-tangle, laver, yam and onion are rich in water-soluble dietary fiber, the daily intake from these vegetables is not much and it is impossible to eat them every day. Therefore, it is a good way to build healthy intestinal tract by taking cream formula to supplement water-soluble dietary fiber.

4 Prescription thoughts and improvements of cream formula

To improve the prescription and preparation process of cream formula, we need to combine the thoughts that cream formula is rich in water-soluble dietary fiber and it is used for "preventing diseases" and regulating chronic diseases.

4.1 *Adding a large amount of water-soluble fiber in cream formula*

The increasing of the water-soluble dietary fiber in cream formula can promote the proliferation of intestinal probiotics.

4.1.1 Paying more attention to the application of herbs that are rich in water-soluble dietary fiber

The top priority of cream formula is tonifying spleen and kidney. So, there is no need to use a large number of herbs in cream formula. According to syndrome differentiation, the reasonable compatibility of herbs in cream formula means that we should value and select the herbs rich in water-soluble fiber on the basis of their primary and secondary effects.These herbs may include yu zhu (*Rhizoma Polygonati Odorati*), huang jing (*Rhizoma Polygonati*), mai dong (*Radix Ophiopogonis*), tian dong (*Radix Asparagi*), ren shen (*Radix Ginseng*), dang shen (*Radix Codonopsis*), huang qi (*Radix Astragalus*), shan yao (*Rhizoma Dioscoreae*), dang gui (*Radix Angelicae Sinensis*), shu di (*Radix Rehmanniae Praeparata*), bai ji (*Rhizoma Bletillae*), hong jing tian (*Radix et Rhizoma Rhodiolae Crenulatae*), tian ma (*Rhizoma Gastrodiae*), bai he (*Bulbus Lilii*), tu si zi (*Semen Cuscutae*), gou qi (*Fructus Lycii*), shan zhu yu (*Fructus Corni*), sang shen (*Mulberry*), hei zhi ma (*Semen Sesami Nigrum*), bai bian dou (*Semen Lablab Album*), yin er (*Tremella*), che qian zi (*Semen Plantaginis*), chen pi (*Pericarpium Citri Reticulatae*), fo shou (*Fructus Citri Sarcodactylis*), zhi qiao (*Fructus Aurantii*), shi hu (*Caulis Dendrobii*), rou cong rong (*Herba Cistanches*), sang ji sheng (*Herba Taxilli*), ling zhi (*Ganoderma*), zhu ling (*Polyporus*) and fu ling (*Poria*), etc.

4.1.2 Paying more attention to the application of medicine-food herbs that are rich in water-soluble dietary fiber

The cream formula made with medicine-food herbs is sweet in taste and mild in nature, which has no harm to spleen and stomach, no toxic and few side effects can be seen so it is good for long-term use. Medicine-food herbs that are rich in water-soluble dietary fiber are as follows: ju ju (*Herba Cichorii*), huang jing (*Rhizoma Polygonati*), yu zhu (*Rhizoma Polygonati Odorati*), bai he (*Bulbus Lilii*), shan yao (*Rhizoma Dioscoreae*), kun bu (*Thallus Eckloniae*), fu ling (*Poria*), ju pi (*Pericarpium Citri Reticulatae*), fo shou (*Fructus Citri Sarcodactylis*), xiang yuan (*Fructus Citri*), xie bai (*Bulbus Allii Macrostemi*), sang shen (*Mulberry*), dao dou (*Semen Canavaliae*), bai bian dou (*Semen Lablab Album*), sha ji (*Fructus Hippophae*), wu mei (*Fructus Mume*), mu gua (*Fructus Chaenomelis*), bai guo (*Semen Ginkgo*), luo han guo (*Fructus Momordicae*), zao (*Fructus Jujubae*), long yan rou (*Arillus Longan*), xing ren (*Semen Armeniacae Amarum*), yu li ren (*Semen Pruni*), zhi ju zi (*Semen Hoveniae*), gou qi zi (*Fructus Lycii*), pang da hai (*Semen Sterculiae Lychnophorae*), tao ren (*Semen Persicae*), hei zhi ma (*Semen Sesami Nigrum*), suan zao ren (*Semen Ziziphi Spinosae*), ren shen (*Radix Ginseng*), dang gui (*Radix Angelicae Sinensis*), gan cao (*Radix et Rhizoma Glycyrrhizae*), mai ya (*Fructus Hordei Germinatus*), zhi

zi (*Fructus Gardeniae)*, dan dou chi (*Semen Sojae Praeparatum*), honey, song hua fen (*Pollen Pini*) and pu huang (*Pollen Typhae*), etc.

4.1.3 Adding food materials that are rich in water-soluble dietary fiber

Food materials that are rich in edible water-soluble dietary fiber can be added in cream formula. These foods include fine powders of chicory, jerusalem artichoke, Chinese artichoke, lycopus lucidus, konjak, sea-tangle and laver, etc.

4.1.4 Making clear cream

We should make clear cream rather than animal cream. Since animals' glue does not contain water-soluble dietary fiber, it is not necessary to use them. Thses animal creams include e jiao (*Colla Corii Asini*), gui jia jiao (*Colla Carapax et Plastrum Testudinis*), bie jia jiao (*Colla Carapacis Trionycis*), lu jiao jiao (*Colla Cornus Cervi*). This can not only reduce costs, but also avoid the high content of animal protein in cream formula, which easily causes corruption.

4.2 *Paying attention to the increasing of diversity of intestinal microflora in cream formula*

Increasing the strains diversity of cream formula can promote the diversity of intestinal probiotics.

4.2.1 Adding the raw honey in when the cream being completely thickened

After the pollen being processed by bees, the honey contains plenty of probiotics such as bacillus and yeasts, etc. The honey is added in when the cream is completely thickened, which can avoid strains death induced by high temperature.

4.2.2 Adding the fermented Chinese medicine in when the cream being completely thickened

We should fully applicate the traditional fermented Chinese medicine. When the is cream completely thickened, the fermented Chinese medicines can be added. This kind of medicine my include liu shen qu (*Massa Medicata Fermentata*), jian shen qu (*Massa Medicata Fermentata*), ban xia qu (*Rhizoma Pinelliae Fermentata*), chen xiang qu (*Chinese Eaglewood Medicated Leaven*), dan nan xing (*Arisaema cum Bile*), dan dou chi (*Semen Sojae Praeparatum*), bai yao jian (*Chinese Gall Leaven*) and hong qu (*Monascus purpureus Went*). In this way the diversity of probiotics strains can be improved .

4.2.3 Adding probiotic living bacteria powder in when the cream being completely thickened

We should fully applicate the modern microecological drugs. When the cream being completely thickened, adding the living bacteria powders and Natto baking powder, such as Bacillus coagulans, Bacillus bifidus, Clostridium butyricum, Bacillus licheniformis, Bacillus cereus, Bacillus subtilis, Enterococcus, can supplement probiotics strains.

4.3 *Paying attention to the applications of herbs with functions of activating blood circulation and removing blood stasis in cream formula*

Herbs with functions of activating blood circulation and removing blood stasis should be fully applied in cream formula. We should not be subject to the old saying of moistning and nourishing.

4.3.1 Adding in the herbs with functions of activating blood circulation and removing blood stasis when the cream is completely thickened

Ggenerally, herbs with functions of activating blood circulation and removing blood stasis contain a variety of active enzymes. When the cream is completely thickened, herbal powders can be selectively added, such as powders of san qi (*Radix et Rhizoma Notoginseng*), chuan xiong (*Rhizoma Chuanxiong*), tao ren (*Semen Persicae*), hong hua (*Flos Carthami*), chi shao (*Radix Paeoniae Rubra*) and dan shen (*Radix et Rhizoma Salviae Miltiorrhizae*). But, animal drugs with functions of activating blood circulation and removing blood stasis could not be used, such as shui zhi (*Hirudo*), di long (*Pheretima*), tu bie chong (*Eupolyphaga seu Steleophaga*), mang chong (*Tabanus*) and qi cao (*Vastabitur Vermibus*).

Adding the insect drugs in cream can easily cause spoilage and these drugs also have heavy smells of fish and mutton.

4.3.2 Adding herbal pollen in when the cream is completely thickened

Herbal pollen is rich in multiple strains, active enzymes and polypeptide. All of these contents have the effect of activating blood and removing blood stasis, which can improve the cardio-cerebrovascular diseases caused by microcirculation disorder, such as atherosclerosis, coronary heart disease and cerebral apoplexy. When the cream is completely thickened, pu huang (*Pollen Typhae*), pine pollen, cedar pollen, camellia pollen and maize pollen could be added.

5 Process improvements of cream formula

To improve and optimize the prescription of cream formula, the adjustment of its process is necessary. In order to maintain strains and enzymes' activities, the scientific improvement and optimization usually are performed at the end of cream thickening.

5.1 *Process improvements of water-soluble dietary fiber*

First, soak and decoct the herbs (e.g. huang jing (*Rhizoma Polygonati*), yu zhu (*Rhizoma Polygonati Odorati*)) that are rich in water-soluble dietary fiber. Next add the food materials (e.g. fine powder of chicory) that are rich in water-soluble dietary fiber when the water decreases to about 35%. Finally, decoct with slow flame until the cream is thickened completely.

5.2 *Process improvements of active strains and enzymes*

In order to keep the strains and enzymes' activities, the raw honey, fermented Chinese medicines, living powder of probiotic, pollen or herbs with functions of activating blood and removing stasis should be added at 40℃ when the water decreases to about 25% at the end of cream thickening. When the clear cream is completely thickened, its water content is about 20%.

6 The present situation of cream formula preparation process

In ancient times, cream formula, for its specific health care and therapeutic efficacy, were used by the rich and high-born people all the time. But the essence and value of cream formula not just refers to the people who use it, but also lies in each process from the prescription to its final thickening.

First, the selected drugs for cream formula are every exquisite. Compatibility of medicines should be made on the basis of the patients' signs and changes of seasons. And the selected drugs are rich in varieties, and most of them are rare medicinal herbs. Cream formula can maximize its medicinal effect only by properly using genuine regional medicinals. Even for the same kind of herb, the differences origins can lead to a considerable difference in active ingredients content. Therefore, if there is no effective quality control measure and traceability of herbs during cream formula preparation process, fake or low-quality herbs can easily be seen as premium ones. Furthermore, the preparation process of traditional cream formula is complex, which includes many processes such as prescribing, soaking, decocting, precipitating, concentrating, thickening, cooling, packing and sealing, etc. However, the preparation process of cream formula in China belongs to backward handicraft production for a long time. This production mode relies on master's experience with miscellaneous and complex processes, which needs great labor intensity. In addition, most production workshops are poor in environmental and hygienic conditions, and have no unified national quality standard, inspection and quality control measures. All of the above can easily cause cheating events, quality and safety risks, and also cause a certain waste to Chinese medicine resources [9]. Some leading pharmaceutical companies pay special attention to the issues above.

6.1 *Lack of systematic theoretical guidance* [10]

As the traditional dosage form, cream formula evolves from the decoction concentration and is still used today. The traditional preparation of the cream formula is the concentration of Chinese medicine extract, which needs to be decocted for a long time and consume high energy. General rules of preparation in Chinese Pharmacopoeia (version 2010) define the cream formula (soft extract) as follows: it is a kind of thick paste prepared by decocting drugs with water and mixing the decoction with refined honey and crystal sugar (or inert sugar). In addition, it also provides that the relative density, insoluble substance, loading capacity and microbial limit of the finished cream should be determined. It can be seen that, from the view of cream preparation process in the Chinese Pharmacopoeia, the qualitative description is more than the quantitative index. Many textbooks are just simply introducing the concept and process of cream formula as well as its preparation processes include soaking, decocting, concentrating, thickening, storing and so on. But, there are no specific and clear rules for each step and preparation process. Related literatures and professional periodicals show that, with different preparation process, the production of cream formula still stays in the exploratory stage. Further theoretical research is needed or guiding the practice.

6.2 *No standard preparation process* [10]

The traditional processing technology of cream formula is complex, time-consuming and slow, so its quality is difficult to control. Through consulting discussions of literatures and professional journals, we found that the preparation methods of cream formula are different and still stay for exploration.

(1) Varieties in soaking and decocting duration, and boiling times. In the preparation of cream formula, soaking duration, decocting duration and growth time of the medicines are important influencing factors. However, during the actual preparation, these factors are entirely and totally different. The analysis of related literatures shows that the soaking duration of the cream formula medicines ranges from 2 h to 12 h, and some even more than 24 h; the decocting times also vary. Take Huang's [11] xiaoban (spot removing) cream formula as an example. The source medicines need to be soaked for 2 h in water, extracted for three times, and decocted for 1h each time. But, in Tiefeng Wang's preparation process, the source medicines need to be soaked for about one night and be decocted with automatic decocting machine[12]. After boiling about 1h, the decoction is extract; then the medicine is decocted twice with hot water, after boiling about 45min, and dregs are squeezed. Finally the decoction is aquired. From the above, we can see that Wang's preparation needs to be soaked for more than 12 h, and decocted for two times. Guolong Gu's et al [13] present that the medicines of cream formula should be put in a large container, then soaked for one night (>12 h) with the cold water above 10～20 cm of the medicines. The next day, the medicines are decoct with mild flame to make the medicines fully expand, then are decocted with strong fire for >1 h. Then the decoction should be filtrated before it is done .The medicines must be decocted repeatedly more than three times until the flavor is light.

So, the soaking duration, decocting duration and growth time of cream formula preparation need to be further researched and speci-

fied.

(2) Lack of quantitative basis for cream-thickening standard cream-thickening. This quantitative basis is very important in cream formula preparation, which will directly influence the properties and quality of the production. Presently, there are several standards to judge cream-thickening: ①Make judgment on "gua qi": when there appear soy-liked bubbles from the bottom of the pot, the cream has been completely thickened. Right now, lift the bamboo slices from the pot, the cream drops down and forms shape of triangle--that is called "gua qi". ②If the cream is not diffuse after dropping on bamboo paper, the cream is completely thickened. ③Minxia Zheng *et al*[14] proposes that we can drop a little cream liquid on absorbent paper and the completely thickened cream won't permeate the paper; or we also can drop a little cream liquid in cold water because the completely thickened cream will form pearls-liked shape. Practical experience shows that "dropping cream liquid into cold water, then forming pearls-liked shape" seems to be the judgment standard of external cream formula. However, the cream made according to this standard is usually overcooked. It is thus evident that the standards above need to be judged by the operator. These standards are non-objective indexes with strong subjective and no exact data control, which needs to be further studied and quantified.

(3) Containers, cooling and storing environments need to be standardized. At present, most containers for cream formula are porcelain and plastic products. Because of the high temperature of the cream after itis completely thickened and it is not possible to box it after cold down, the impact of temperature should be considered when choosing containers. The cooling and storing of the cream formula are very essential too, because a little carelessness may make the cream become mildewed. Therefore, in consideration of the guarantee of the product's quality and storage, effective quality control should be performed in all steps including production environment, container sanitary environment, cooling and storage environment.

6.3 *The intake dosage of the cream formula needs to be quantified accurately* [10]

At present, the usual taking dosage of cream formula is 2 times/d,1 tablespoons/time, which can be eaten directly or taken with boiled warm water. Some also suggests taking about 10 g/time or20-30 ml/time. Now, the undefined taking dosage of cream formula is not in line with the modern dosage specification. After analyzing the effect, we found the cream taking of each time should be regularly quantified. Moreover, the taking dosage should be quantitatively analyzed to determine the quantity and total amount of each day and the whole course. How to make the cream being convenient for use, stable in nature and accurate for single dose are tasks faced by pharmaceutical researchers. Currently, the new numerical control packaging machine can carry out adjustable dose packaging for cream formula, which should be studied and developed.

6.4 *Uncertainty of personnel qualification* [10]

Nowadays, the state has no clear management on cream formula preparation practitioners, nor has the qualified requirements on physicians and pharmacists. As the taking duration of cream formula is long, generally about 2 months, a serious impact will be produced on patients if there are some problems in cream formula or its use is not symptomatic. So, the relevant departments should pay more attention to the potential quality issues of cream formula.

6.5 *Lack of quality supervision in cream formula preparation* [10]

Presently, the cream formula preparation has been widely carried out throughout the country, but there is no unified supervision, clear laws and regulations on production of cream formula. According to a report, the Chinese Medicine Industry Association in some areas has formulated the management methods for cream formula preparation. But these methods only play a self-discipline role within the associations, which can't be applied to the whole industry. The enterprise can only guarantee the cream quality by the supervision of its own preparation process. In a word, the unique bar code can achieve real-time monitoring and precise tracing, which can fully guarantee the quality of the cream formula. Now, it is still a question for us to think about how to effectively supervise the cream preparation quality throughout the whole industry.

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