Study on Medication Regularity of Sijunzi Decoction and Its Categorized Prescriptions Based on Attribute Partial Order Structure Diagram

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Abstract. Sijunzi decoction is a famous prescription in traditional Chinese medicine (TCM) for the treatment of spleen deficiency syndrome. Spleen deficiency syndrome is manifested in a variety of symptoms. Herbs can be added or replaced on the basis of Sijunzi decoction according to different symptoms, forming Sijunzi categorized prescriptions. In this paper, the medication regularity of Sijunzi decoction and its categorized prescriptions was studied based on attribute partial order structure diagram (APOS D). According to prescription-herb APOS D generated from Sijunzi decoction categorized prescriptions screened from comprehensive TCM database, it can be seen that three herbs are used in all prescriptions, i.e. Renshen, Baizhu and Fuling. Different forms of Sijunzi decoction mainly depend on whether the forth herb is Zhigancao, Chenpi-Gancao, or Gancao. The efficacy of common herbs in the prescriptions for different symptoms can be presented by prescription-herb APOS D and prescription-symptom APOS D generated from different prescription subgroups. The experimental results show that APOS D can effectively reveal the medication regularity of Sijunzi decoction and its categorized prescriptions, and it is an useful tool for theoretical study of TCM.

1. Introduction
Sijunzi decoction is a famous prescription for the treatment of spleen deficiency syndrome in traditional Chinese medicine (TCM). The composition of the prescription is Renshen, Baizhu, Fuling and Gancao. Any single herb in the prescription can not achieve effective treatment effect, while cooperative use of the four drugs in Sijunzi decoction can play the role of invigorating spleen and assisting stomach to transport[1]. Spleen deficiency syndrome can be clinically manifested as various symptoms. Adding or changing herbs on the basis of Sijunzi decoction can achieve the treatment effect for different symptoms. Therefore, it is of great significance to study different forms of composition of Sijunzi decoction according to different symptoms in order to reveal medication regularity of spleen deficiency syndrome.

More and more data mining methods have been applied to study medication regularity of TCM[2]. Liu employed frequency statistics, association rules and network atlas analysis methods to explore laws of using peach kernel in prescriptions[3]. The association rules and entropy clustering algorithm are selected by Pan to analyze compatibility rule of herb Danggui[4]. Lin applied frequency statistics and cluster analysis to analyze the rules of prescription for treatment of cystitis glandularis from
spleen[5]. Although many methods have extracted some medication regularities, the process of discovering rules is not visible, which is not conducive to integrating TCM expert’s knowledge.

A new knowledge visualization method called attribute partial order structure diagram (APOSĐ) is proposed by Hong[6] based on the formal concept analysis theory. APOSĐ has the characteristics of distinct hierarchical structure, no cross lines and subgroups of clustering, which make it well applied in the fields of syndrome differentiation and compatibility of TCM prescriptions[7-9]. In this paper, APOSĐ is applied to study different forms of Sijunzi decoction for different symptoms, so as to provide valuable reference to theoretical research of spleen deficiency syndrome.

2. Theory of Attribute Partial Order Structure Diagram

APOSĐ can present coverage relationships between objects and attributes, calculate common attributes and specific attributes, and clustering objects with certain attributes. These functions beneficial for APOSĐ discovering knowledge from its overall and local structures. Constructing APOSĐ must start from formal context. A formal context is a triple \( K = \{ U, M, I \} \). \( U \) is a set of objects, \( M \) is a set of attributes, and \( I \) is a set of binary relations reflecting whether an object has an attribute. Usually, a formal context is presented by a crosstab, as shown in table 1. The rows of the crosstab correspond to different objects, and the columns of the crosstab correspond to different attributes. If an object has an attribute, the cell where the object and the attribute intersects is marked with a symbol “×”.

|    | a | b | c | d | e | f |
|----|---|---|---|---|---|---|
| O1 | × | × |   | × |   |   |
| O2 | × |   | × |   |   |   |
| O3 | × | × | × |   | × |   |
| O4 | × | × | × | × | × | × |
| O5 | × | × | × | × |   |   |

Table 1. An Example of a formal context.

APOSĐ forms a hierarchical structure according to coverage relationships of attributes to objects. There is only one vertex, called the largest common attribute, which covers all objects. For example, attribute \( a \) in table 1 is the largest common attribute. If there is no such largest common attribute, the label of vertex is not marked. Other nodes in APOSĐ are arranged hierarchically according to the degree of coverage of attributes over objects. According to different degree of attributes covering objects, some attributes are defined as follows[10]:

Definition 1 (Opposite attribute) In the formal context \( K = \{ U, M, I \} \), if attributes \( m_i \) and \( m_j \) satisfy \( g(m_i) \cup g(m_j) = U \) and \( g(m_i) \cap g(m_j) = \phi \), \( m_i \) and \( m_j \) are called opposite attributes.

Definition 2 (Mutually non-inclusive attributes) In the formal context \( K = \{ U, M, I \} \), \( m_i, m_j \in M, \ i \neq j \), if \( g(m_i) \cap g(m_j) \neq \phi \) and \( g(m_i) \nsubseteq g(m_j) \wedge g(m_j) \nsubseteq g(m_i) \), \( m_i \) and \( m_j \) are called mutually non-inclusive attributes.

Definition 3 (Associated attributes) In the formal context \( K = \{ U, M, I \} \), if attributes \( m_i \) and \( m_j \) satisfy \( g(m_i) \subseteq g(m_j), \ i \neq j \), attribute \( m_i \) is associated attributes of attributes \( m_j \).

The first layer of APOSĐ is composed of nodes of opposite attributes. If there are no opposite attributes, the least mutually non-inclusive attributes that can cover all objects are selected as the nodes of this layer. For example, because there are no opposite attributes in table 1, the mutually non-inclusive attributes \( b \) and \( c \) in table 1 form the first layer of APOSĐ. The associated attributes are arranged in the adjacent upper and lower layers in APOSĐ according to their degree of coverage. For example, attribute \( b \) is associated attribute of attribute \( c \) in table 1, attribute \( b \) is at the upper
layer of attribute \( e \) for attribute \( b \) covers more objects. There’s a directional edge from vertex to each node on the first layer. The following layers of APOSĐ can be generated according to the above method. The nodes near bottom of APOSĐ are usually unique attributes. That is, these attributes cover only one object. For example, attribute \( f \) in table 1 is a unique attribute.

3. Experimental Results

Knowledge discovery was carried out by analyzing prescription-herb APOSĐ and prescription-syndrome APOSĐ of different forms of Sijunzi decoction screened from TCMID database[11]. The alias or specific names of herbs and symptoms in 67 screened prescriptions were all set as uniform names. The nodes on upper layers of APOSĐ are commonly used attributes with universal significance. Therefore, only nodes on upper layers of APOSĐ are analyzed below. The upper layers in prescription-herb APOSĐ of 67 prescriptions is shown in figure 1. It can be seen from figure 1 that herbs \{Renshen, Baizhu, Fuling\} are the largest common attributes. That is, they are common herbs used by all 67 prescriptions. The first layer of APOSĐ is composed of three nodes \{Zhigancao, Chenpi-Gancao, Gancao\}, each of which leads a subgroup structure. There are 48 prescriptions covered by node \{Zhigancao\}, 11 prescriptions covered by node \{Chenpi-Gancao\} and 8 prescriptions covered by node \{Gancao\}. It can be seen from vertex and the first layer of APOSĐ that three herbs in Sijunzi decoction is fixed, and different forms mainly depend on whether the forth herb is Zhigancao, Chenpi-Gancao or Gancao. From the number of prescriptions they covered, Zhigancao is more commonly used than Chenpi-Gancao or Gancao.

The subgroup structure lead by node \{Gancao\} is very similar to that lead by node \{Chenpi-Gancao\}. In order to analyze these two subgroups more clearly, knowledge discovery was carried out by analyzing prescription-herb APOSĐ and prescription-symptom APOSĐ of these two subgroups respectively.

3.1. Knowledge discovery of Gancao subgroup

The upper layers of Gancao subgroup in figure 1 is extracted, as shown in figure 2. The herbs on the upper two layers are Muxiang, Chenxiang, Danggui, Baishao, Huangqi, Baihe, Sharen, Dingxiang and Shanzhuyu. Muxiang and Chenxiang are used as qi regulating herbs. Danggui, Baishao, Huangqi and Baihe are reinforcing deficiency herbs. Shanren has the effect of dissipating dampness. Dingxiang can warm the interior. Shanzhuyu is the astringent herb. Therefore, when Gancao is used as the forth herb in Sijunzi decoction, it is mainly compatible with reinforcing deficiency herbs.

The prescription-symptom APOSĐ of Gancao subgroup is shown in figure 3. As can be seen from figure 3, the common symptoms in indications of Gancao subgroup are anorexia, abdominal distension...
(AD) and marasmus. The symptom dry mouth (DM) and symptom phlegm also appeared in some prescriptions, which corresponds to heat-clearing and reducing phlegm effect of Gancao.

3.2. Knowledge discovery of Chenpi-Gancao subgroup

The upper layers of Chenpi-Gancao subgroup in figure 1 is extracted, as shown in figure 4. In figure 4, there are three small subgroups under the nodes \{Chenpi-Gancao\}, which are lead by nodes \{Houpo\}, \{Banxia\} and \{Shanyao-Zexie\}. The prescriptions-symptoms APOSD of Chenpi-Gancao subgroup is shown in figure 5. As can be seen from figure 5, the common symptoms in indications of Chenpi-Gancao subgroup are eating less (EL), loose stool (LS) and phlegm. The symptom EL appeared in all indications of Houpo subgroup, which corresponds to removing fullness effect of Houpo. The symptom LS appeared in all indications of Shanyao-Zexie subgroup, which corresponds to stopping diarrhea effect of Shanyao-Zexie herb pairs. The symptom phlegm appeared in all indications of Banxia subgroup, which corresponds to reducing phlegm effect of Banxia.
4. Conclusion
APOSD can clearly express the relationship between attributes and objects for knowledge discovery. In this paper, APOSD is employed to extract knowledge from prescription-herb APOSD and prescription-symptom APOSD of Sijunzi decoction and its categorized prescriptions screened from TCMID database. According to prescription-herb APOSD, Renshen, Baizhu and Fuling are used in all prescriptions. Different forms of Sijunzi decoction mainly depend on whether the forth herb is Zhigancao, Chenpi-Gancao, or Gancao. For Gancao subgroup and Chenpi-Gancao subgroup, comprehensive analysis of prescription-herb APOSD and prescription-symptom APOSD can clarify herb efficacy for different symptoms. APOSD provides a powerful tool for theoretical research on TCM. Further research will focus on knowledge discovery by APOSD of dose-effect relationship for different TCM syndromes.

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References
[1] Lin C H. (2018) Clinical Application of Sijunzi Decoction in Spleen-Stomach Qi Deficiency Syndrome of Internal Medicine Diseases of Traditional Chinese Medicine. Capital Food Medicine, 25: 173.
[2] Jiang Z B. (2015) Research Method of Prescription Compatibility Law Based on Data Mining. Nanjing University of Traditional Chinese Medicine.
[3] Liu J L, Pei L, Wang W K, et al.. (2019) Study on Compatibility Law of Taoren Prescription Based on Data Mining. Jiangsu Traditional Chinese Medicine, 51: 65-68.
[4] Pan W. (2015) Analysis of Compatibility Rules of Core Drugs and Prescription-pattern of Primary Dysmenorrhea Based on Data Mining. Western Journal of Traditional Chinese Medicine, 28: 75-77.
[5] Lin M Q, Xu J H. (2019) Data Mining and Cluster Analysis for Retrospective Analysis of the Regularity of Treatment and Drug Use of Cystitis Glandularis from Spleen. Massage and Rehabilitation Medicine, 49-50+52.
[6] Hong W X, Luan J M, Zhang T, et al.. (2014) Knowledge discovery method based on the theory of partial order structure. Journal of Yanshan University, 38: 394-402.
[7] Yan E L, Song J L, Liu C N, et al.. (2017) A Research on Syndrome Element Differentiation Based on Phenomenology and Mathematical Method. Chinese Medicine, https://doi.org/10.1186/s13020-017-0141-1.
[8] Song J L, Yu J P, Yan E L, et al.. (2013) Syndrome Differentiation of Six Meridians for Warm Disease Based on Structural Partial-Ordered Attribute Diagram. ICIC Express Letters, 7: 947-952.
[9] Fan F J, Hong W X, Song J L, et al.. (2016) Visualization Method and Knowledge Discovery of Prescription Composition. Chinese Journal of Biomedical Engineering, 35: 764-768.
[10] Hong W X, Luan J M, Zhang T, et al.. (2014) Complete definition of attribute feature and object feature in formal context. Journal of Yanshan University, 38: 381-387.
[11] Center for Bioinformatics and Computational Biology, East China Normal University. (2014) Traditional Chinese Medicines Integrated Database. http://www.megabionet.org/tcmid/