



# Analysis of Medication in 3925 Outpatient Prescriptions Containing Traditional Chinese Medicine Toosendan Fructus

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**Abstract:** This study investigates the clinical application and safety of Toosendan Fructus to provide evidence for its rational use in practice. A total of 3,925 outpatient prescriptions containing Toosendan Fructus were collected from January to December 2023 at Guangzhou Hospital of Integrated Chinese and Western Medicine. Data on patient demographics, diagnosis, department distribution, dosage, and herb combinations were analyzed. Among 2,951 patients, 1,697 were female (1.35 times that of male). Most patients (52.18%) were aged 19–44 years. The Liver disease department prescribed the most Toosendan Fructus (28.87%), primarily for liver stagnacy (22.52%). Stir-fried Toosendan Fructus was used in 95.18% of prescriptions, with 64.84% exceeding the Chinese Pharmacopoeia limit (>10 g). Common combinations included *Paoniae Radix Alba*, *Bupleuri Radix*, and vinegar-processed *Rhizoma Corydalis*. Stir-frying and compatible use of Chinese materia medica can reduce the toxicity of Toosendan Fructus. However, an audit system for off-label use and enhanced medication monitoring are recommended to ensure clinical safety.

**Keywords:** Toosendan Fructus; analysis on prescription medication; rational medication

## 1. Introduction

Toosendan Fructus is the dried mature fruit of *Melia toosendan* Sieb. et Zucc. with a bitter taste and cold nature. It is slightly toxic and enters the liver, small intestine, and bladder. It has the effects of soothing the liver to clear heat, promoting qi circulation to relieve pain, and killing parasites[1]. Current research on its detoxification primarily focuses on two strategies: processing-induction and compatibility-medication[2, 3]. In clinical application, the stir-frying method recorded in the Chinese Pharmacopoeia (2025 edition) is commonly adopted. Stir-fried Toosendan Fructus not only mitigates its bitter-cold properties and reduces its potential to cause loose stools, but also enhances its function of regulating qi to alleviate pain[4].

This study collected outpatient prescriptions using traditional Chinese medicine (TCM) from Guangzhou Hospital of Integrated Traditional Chinese and Western Medicine (hereinafter referred to as “the hospital”). By retrospectively analyzing the basic patient information, diagnoses, departments, as well as the type, dosage, and compatibility of Toosendan Fructus in prescriptions from 2023, we investigated its patterns of clinical application. The aim is to provide a scientific basis for the rational use of Toosendan Fructus.

## 2. Materials and methods

### 2.1 Data collection

A total of 3925 outpatient prescriptions containing Toosendan Fructus from January 1 to December 31 in 2023, were retrieved through the hospital information management system. Each prescription included information such as patient gender, age, consultation date, department, medical diagnosis, disease and syndrome pattern by TCM, prescribed medications, usage, and dosage.

### 2.2 Prescription standardization

The information regarding the constituents, diseases and syndromes of TCM in the prescriptions was standardized according to national standards. The names of Chinese medicinal materials were standardized with reference to the Pharmacopoeia of the People's Republic of China (2025 edition)[1]. TCM syndromes and diseases were standardized with reference to Clinic terminology of traditional Chinese medical diagnosis and treatment—Part 2: Syndromes/patterns (GB/T 16751.2-2021)[5] and Part 1: Diseases (GB/T 16751.1-2023)[6], respectively.

## 2.3 Data analysis

Microsoft Excel software was used for statistical analysis of the usage patterns of Toosendan Fructus based on the commonly used types of processed products, patient age, gender, and department distribution. By examining the dosage of Toosendan Fructus, the total prescription dosage, and compatibility with other TCMs, the medication patterns and existing problems in the outpatient prescriptions containing Toosendan Fructus at the hospital were identified. These findings were then analyzed, and corresponding intervention measures were explored.

## 3. Results

### 3.1 Basic information of patients using Toosendan Fructus

Patients were categorized according to the World Health Organization (WHO) age groups: school age (6–12), adolescence (13–18), young adulthood (19–44), middle age (45–59), and old age ( $\geq 60$ ). The results showed that the average age of patients using Toosendan Fructus was 44. Patients in the young adulthood group constituted the largest proportion of users, with 2,048 cases (52.18%), followed by those in the middle age as shown in Table 1. The youngest patient was 6 years and 8 months old, and the oldest was 92 years old. Across all age groups, the number of female patients using Toosendan Fructus was higher than that of male patients, with the total number of female patients being approximately 1.35 times that of male patients.

**Table 1. Age and gender distribution of patients in the 3925 prescriptions containing Toosendan Fructus**

Age	Type of Toosendan Fructus		Gender		Total (n)	Percentage (%)
	Unprocessed (n)	Stir-fried (n)	Male (n)	Female (n)		
School age (6–12)	0	23	9	14	23	0.59
Adolescence (13–18)	2	80	21	61	82	2.09
Young adulthood (19–44)	85	1963	886	1162	2048	52.18
Middle age (45–59)	67	1195	553	709	1262	32.15
Old age ( $\geq 60$ )	35	475	195	315	510	12.99
Total	189	3736	1664	2261	3925	100.0

### 3.2 Departmental distribution of prescriptions containing Toosendan Fructus

Statistical analysis revealed that Toosendan Fructus were used in prescriptions from 44 different outpatient departments, covering nearly half of all outpatient departments. The liver disease department had the highest frequency of use, with 1,133 prescriptions, accounting for 28.87% of the total. This was followed by the general internal medicine department (642 prescriptions, 16.36%) and the preventive treatment department (599 prescriptions, 15.26%), as detailed in Table 2.

**Table 2. Departmental distribution of prescriptions containing Toosendan Fructus (>100)**

Rank	Department	Number of prescriptions	Percentage (%)
1	Liver disease department	1133	28.87
2	General internal medicine department	642	16.36
3	Preventive treatment department	599	15.26
4	Gastroenterology department	414	10.55
5	Breast specialty department	240	6.11
6	General surgery department	206	5.25
7	Psychological sleep department	100	2.55

### 3.3 Clinical diagnoses in prescriptions containing Toosendan Fructus

As shown in Table 3, among the TCM diagnoses in prescriptions containing Toosendan Fructus, liver stagnacy was the most frequent, with 884 prescriptions (22.52%), followed by abdominal pain, stomach stuffiness disease, breast lump, and insomnia. The top five syndrome patterns were liver depression and spleen deficiency, with 836 prescriptions (21.30%), followed by qi stagnation due to liver depression, disharmony of liver and stomach, liver and spleen disharmony, and dampness and heat in the liver and gallbladder. Regarding diseases treated with Toosendan Fructus, liver diseases were the most frequent, with a high of 929 prescriptions (23.67%), followed by chronic gastritis, sleep disorders and et al. (see Table 3).

**Table 3. Top 10 diagnoses, syndrome patterns, and diseases in prescriptions containing Toosendan Fructus**

NO.	Diagnoses by TCM	Number of prescriptions	Syndrome patterns	Number of prescriptions
1	Liver stagnacy	884	Liver depression and spleen deficiency	836
2	Abdominal pain	394	Qi stagnation due to liver depression	722
3	Stomach stuffiness disease	317	Disharmony of liver and stomach	310
4	Breast lump	225	Liver and spleen disharmony	110
5	Insomnia	222	Dampness and heat in the liver and gallbladder	107
6	Epigastralgia	213	Qi stagnation and blood stasis	100
7	Depression disease	187	Spleen deficiency	100
8	Gallbladder distension	138	Spleen deficiency with dampness encumbrance	85
9	Mass due to qi stagnation	109	Spleen and stomach deficiency	81
10	Hypochondriac pain	107	Spleen deficiency with dampness and heat	78

### 3.4 Usage of Toosendan Fructus in outpatient prescriptions

#### 3.4.1 Commonly used medication types and dosage

In 2023, two types were used in the outpatient TCM prescriptions: unprocessed Toosendan Fructus and stir-fried Toosendan Fructus. The majority of prescriptions used the processed Stir-fried Toosendan Fructus, totaling 3,736 cases (95.18%), while only 189 prescriptions (4.82%) specified the unprocessed form, as shown in Table 4.

#### 3.4.2 Dosage, administration frequency, and medication duration

The most commonly used dosage of Toosendan Fructus was 18 g, accounting for 62.70% of prescriptions, while the overall dosage range was 3 g to 20 g (Table 4). The Pharmacopoeia of the People's Republic of China (2025 edition) specifies a single-dose range of 5–10 g for Toosendan Fructus as safe[1]. In 2023, only 1,379 prescriptions (35.13%) from this hospital fell within this specified range (Table 4). For internal administration, the most commonly used dosage range was 15–20 g, all involving stir-fried Toosendan Fructus and exceeding the specified limit by approximately 10 g. Prescriptions using unprocessed Toosendan Fructus all complied with the specified dosage range.

**Table 4. Dosage ranges and administration of Toosendan Fructus in single prescription**

Range & dosage of single prescription	Unprocessed Toosendan Fructus (n)	Stir-fried Toosendan Fructus (n)	Total (n)	Percentage (%)
<5 g	3 g	0	1	0.03
	5 g	101	229	8.41
5 ~ 10 g	6 g	0	3	0.08
	10 g	88	958	26.65
>10 ~ 15 g	12 g	0	1	0.03
	15 g	0	80	2.04
>15 ~ 20 g	18 g	0	2461	62.70
	20 g	0	3	0.08
Total	189	3736	3925	100.0

Overall, the most common administration frequency for prescriptions containing Toosendan Fructus was twice daily (BID), involving 2,951 prescriptions (75%), followed by once daily (QD). Only one prescription indicated three times daily (TID). Specifically, for prescriptions using Stir-fried Toosendan Fructus, the primary frequency was BID (2,909 prescriptions, 77.86%). For prescriptions using unprocessed Toosendan Fructus, the primary frequency was QD (147 prescriptions, 77.78%), as shown in Table 5. The medication duration for prescriptions containing Toosendan Fructus ranged from 1 to 15 days, with most prescriptions being for 7 days or less. Duration of 1, 2, 3, 5, and 7 days were more common, with 1 day (1,010 prescriptions) and 2 days (1,040 prescriptions) being the most frequent. Prescriptions exceeding 7 days were fewer, less than 100 in total (Table 5).

**Table 5. Administration frequency and medication duration for Toosendan Fructus in TCM prescriptions**

Type	Administration frequency (Prescriptions, n)			Medication duration (Prescriptions, n)							
	QD	BID	TID	1 day	2 days	3 days	4 days	5 days	6 days	7 days	> 7 days
Unprocessed Toosendan Fructus	147	42	0	0	3	26	20	57	4	67	12
Stir-fried Toosendan Fructus	826	2909	1	1010	1037	385	153	412	42	613	84
Total	973	2951	1	1010	1040	411	173	469	46	680	96

### 3.4.3 Compatible applications of Chinese materia medica

The outpatient prescriptions containing Toosendan Fructus was combined with at least 6 other TCMs, up to a maximum of 24. The frequency ranking of Chinese medicines combined with Toosendan Fructus is shown in Table 6. Paeoniae Radix Alba (Bai Shao), Bupleuri Radix (Bei Chai Hu), and vinegar-processed Corydalis Rhizoma (Cu Yan Hu Suo) were the most frequently combined herbs with Toosendan Fructus. Furthermore, prescriptions containing unprocessed Toosendan Fructus also commonly combined Poria (Fu Ling) and Atractylodis Macrocephalae Rhizoma (Bai Zhu). In contrast, those containing the stir-fried form frequently paired with vinegar-processed Cyperi Rhizoma and Curcumae Radix.

**Table 6. Top 10 Chinese medicines combined with Toosendan Fructus in outpatient prescriptions**

NO.	Prescriptions containing unprocessed Toosendan Fructus (189)			Prescriptions containing stir-fried Toosendan Fructus (3736)		
	Compatibility of Chinese medicine	Prescriptions (n)	Percentage(%)	Compatibility of Chinese medicine	Prescriptions (n)	Percentage (%)
1	Paeoniae Radix Alba	148	78.31	Paeoniae Radix Alba	3328	89.08
2	Bupleuri Radix	136	71.96	Bupleuri Radix	3326	89.03
3	Vinegar-processed Corydalis Rhizoma	131	69.31	Vinegar-processed Corydalis Rhizoma	3188	85.33
4	Poria	127	67.20	Vinegar-processed Cyperi Rhizoma	2985	79.90
5	Atractylodis Macrocephalae Rhizoma	118	62.43	Curcumae Radix	2936	78.59
6	Bran-fried Aurantii Fructus	98	51.85	Glycyrrhizae Radix et Rhizoma	2849	76.26
7	Artemisiae Scopariae Herba	88	46.56	Steamed Citri Reticulatae Pericarpium	2836	75.91
8	Cyperi Rhizoma	82	43.39	Bran-fried Aurantii Fructus	2795	74.81
9	Citri Reticulatae Pericarpium	76	40.21	Angelicae Sinensis Radix	2742	73.39
10	Chuanxiong Rhizoma	65	34.39	Chuanxiong Rhizoma	2550	68.25

## 4. Discussion

### 4.1 Analysis of outpatient application of Toosendan Fructus

Despite the variety of traditional processing methods for Toosendan Fructus (e.g., salt-, stir-frying, and vinegar-processing)[7], only the cleansed and stir-fried forms were used in outpatient pharmacy of the hospital, aligning with the simplified standards of the Chinese Pharmacopoeia (2025 edition)[1]. Stir-fried Toosendan Fructus, which accounted for over 95% of clinical use, is preferred due to its reduced toxicity. This is particularly relevant for vulnerable populations like children and the elderly, who have weaker metabolic capacity. Studies confirm that stir-frying significantly reduces total triterpenoids (e.g., toosendanin), thereby mitigating toxic reactions like liver injury and gastrointestinal irritation[4].

Overall, Toosendan Fructus is widely applied across multiple departments, most frequently in liver diseases (28.87% of cases), for its efficacy in soothing the liver and regulating qi. Its use primarily targets patterns of liver depression and spleen deficiency, demonstrating marked effects in relieving depression and pain. These therapeutic outcomes are supported by integrated traditional Chinese and Western medicine research, confirming its value in treating liver disorders caused by qi stagnation and blood stasis.

## 4.2 Characteristics of clinical dosage of Toosendan Fructus

In the 3,925 prescriptions from the hospital, the single dosage of Toosendan Fructus generally ranged from 5 g to 20 g. Specifically, the stir-fried form was commonly administered at 15–20 g per dose. All dosages of unprocessed Toosendan Fructus used in the hospital fell within ranges documented in both classical texts and modern clinical practice. To date, no poisoning or adverse reactions related to its use have been reported based on physician–patient communications. Comparatively, overdosing is less frequently reported in other hospitals[8, 9], this is likely because they primarily use the unprocessed herb, which has higher toxicity. Consequently, clinicians naturally exercise greater caution in dosing.

Notably, while the dosage of stir-fried Toosendan Fructus in this hospital exceeded the limit recommended by the Chinese Pharmacopoeia, studies suggest that stir-frying alters the intestinal absorption of toosendanin and mitigates mitochondrial dysfunction, thereby reducing its toxicity[4]. As a result, the stir-fried form can be more safely applied in vulnerable populations, including the elderly, children, and patients with impaired liver or kidney function.

## 4.3 Analysis of the patterns of clinical compatibility of Toosendan Fructus

The combination of Toosendan Fructus with different herbs can better exert the synergistic effects of Chinese medicine, reduce its own toxic and side effects, lessen the burden on the body, and better achieve therapeutic outcomes[10, 11]. From the frequency statistics, *Paeoniae Radix Alba*, *Bupleuri Radix*, and vinegar-processed *Corydalis Rhizome* are commonly used herbs combined with Toosendan Fructus, with the proportion of prescriptions containing these combinations being  $\geq 65\%$ .

*Paeoniae Radix Alba* nourishes and softens the liver, enable the liver to perform its draining function. Toosendan Fructus is a qi-regulating herb that can alleviate or stop pain. Studies show that compared to administering a distillate of Toosendan Fructus alone, the combination with *Paeoniae Radix Alba* can increase the content of tumor necrosis factor and interleukin-6, promote liver gene expression, and reduce the liver injury caused by Toosendan Fructus. This combination utilizes herbs with similar functions to reduce toxicity and correct the bias of the medicine[12].

*Bupleuri Radix* is often used as the monarch herb in formulations and is commonly used clinically in TCM for treating digestive diseases, immune or circulatory system diseases. It was found that the liver-protective effect of *Bupleurum Chinense* (Bei Chai Hu) was stronger than that of *Bupleurum Scorzoniferifolium* (Nan Chai Hu), while the latter had better lipid-lowering efficacy[13]. Vinegar-processing enhances the effect of *Bupleuri Radix* on draining liver and gallbladder, allowing better functioning of liver and gallbladder metabolism. Toosendan Fructus can disperse and move stagnant liver qi to relieve pain. Chinese Thorowax Root and Toosendan Fructus coordinate with each other, enabling better treatment of liver metabolism diseases and also reducing the hepatotoxicity of Toosendan Fructus.

*Corydalis Rhizome* can regulate qi movement in the blood and treat various pains throughout the body. Vinegar-processing enhances its own pain-relieving effect. Toosendan Fructus itself has a strong effect on alleviating or stopping pain. *Corydalis Rhizome* and Toosendan Fructus are important herbs in the *Jin Ling Zi San*. Observing the anti-inflammatory and analgesic effects of different processed products in this formula using the hot-plate test and inflammatory mouse models revealed that the combination of processed *Corydalis Rhizome* and Toosendan Fructus had similar effects in combating inflammatory factors and analgesia, and they coordinated to exert better pain-relieving effects[14].

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