

# Detection and Analysis of the Quality of Ibuprofen Granules

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**Abstract.** The Ibuprofen Granules comprehensive quality testing to ensure that it is in accordance with the provisions of Chinese pharmacopoeia. With reference of Chinese pharmacopoeia, the Ibuprofen Granules is tested by UV, HPLC, in terms of grain size checking, volume deviation, weight loss on drying detection, dissolution rate detection, and quality evaluation. Results indicated that Ibuprofen Granules conform to the standards. The Ibuprofen Granules are qualified and should be permitted to be marketed.

## 1. Introduction

The chemical formula of ibuprofen is  $C_{13}H_{18}O_2$ , The active ingredient is 2 - ( 4 - strange ) propionic acid. It is a kind of aromatic benzene acid derivatives, belongs to the nervous system medicine<sup>[1]</sup>. It is an important nonsteroidal anti - inflammatory drug ( NSAIDs ) developed in the 1960s. It has a strong effect, good curative effect and low toxicity, and is widely used in clinic<sup>[2]</sup>. The research and development of its preparation and dosage form is also in the high tide stage, the common dosage form of ibuprofen preparation has sustained release capsule, sustained release matrix tablet<sup>[3]</sup>, liniment, tablet, effervescent tablet<sup>[4]</sup>. Clinically, it is safe and effective for Antipyretic, although the analgesic effect is stronger than aspirin, Phenylbutazone or acetaminophen, but the mechanism of anti-inflammatory and analgesic effect has not been completely clarified. One of the common skin reactions in the side effects of ibuprofen is itching, occasionally ulceration and bleeding and skin rash, and stimulation to the gastrointestinal tract<sup>[5]</sup>.

## 2. Materials and apparatus

Ibuprofen granules, ibuprofen reference substance, ibuprofen impurity B、Ibuprofen granules, ibuprofen reference substance, ibuprofen impurity A、J、N. UV - vis spectrophotometer, intelligent drug dissolution tester, high performance liquid chromatography, ultrasonic cleaning machine, electronic balance.

## 3. Methods

### 3.1 Identification of ibuprofen granules

The maximum absorption of ibuprofen in the wavelength of 265 nm and 273 nm was found at the wavelength of 245 nm and 271 nm. There was a shoulder peak at the wavelength of 259 nm<sup>[6]</sup>.



### 3.2 Examination of ibuprofen granules

**3.2.1. Determination of the characteristics of Ibuprofen granules.** The appearance of ibuprofen granules was observed<sup>[7]</sup>.

**3.2.2 Examination of particle size of ibuprofen granules.** According to the particle size and particle size distribution determination method, can not pass the number of sieve 1 and can pass the sum of 5 sieve not more than 15% of the test amount<sup>[8]</sup>.

**3.2.3 Examination of the difference of the amount of ibuprofen granules.** According to the weight of each bag, the contents and average contents of each bag are calculated according to the weight of each bag, the difference between the amount of each bag and the average load is  $\pm 8\%$ <sup>[9-10]</sup>.

**3.2.4 Examination of weight loss on drying detection of ibuprofen granules.** Weigh two samples, 60°C vacuum drying to constant weight, less loss of weight less than 2.0%<sup>[11]</sup>.

**3.2.5 Examination of dissolution rate detection of ibuprofen granules.** The water temperature was 37 °C, and 6 bags of the ibuprofen granules were input into 6 drying turn. the absorbance was determined by UV - visible spectrophotometry at the wavelength of 222 nm. the absorbance absorption coefficient was 1 cm 1 cm 1 cm, and the limit was not less than 70% to the mark.  $P\% = \frac{A \times 10 \times n}{E_{1\text{cm}}^{1\%} \times B} \times 100\%$  A: The peak area or absorbance of the sample solution; n: Sample dilution

multiple; B: Sample mark content<sup>[12-14]</sup>.

### 3.3 Examination of dissolution rate detection of ibuprofen granules

**3.3.1 Solution preparation.** Preparation of test solution. Take the right amount of the product into a 100 mL bottle, add 30 mL of methanol, shake for 30 minutes and add 30 ml of methanol. Shake and filter water with water for sample solution; Preparation of contrast solution A: Carefully measure 1 mL of the sample solution into a 100 mL bottle and dilute it with a flow phase a ( phosphoric acid - acetonitrile - water 0.5 mL: 400 mL: 600 mL ) to the scale, shake well. Suck 1 mL of the solution in a 10 mL bottle and dilute to the scale as a reference solution a with a flow phase a; Preparation of contrast solution B: Take appropriate amount of ibuprofen impurity B in a 10 mL amount bottle, and dilute to the scale with acetonitrile as solution A; The ibuprofen reference substance was accurately measured 20 mg in a 10 mL bottle, with acetonitrile 2 mL dissolved, and then added 1 mL of solution a diluted to the scale as a control solution B with a flow phase A; Preparation of contrast solution C: The mixture of a bottle containing impurity A j and n was dissolved with 1 mL of acetonitrile and transferred to a 5 mL volumetric flask and diluted to the scale with a flow phase a as a reference substance solution C.

**3.3.2 Detection condition and method.** Column. C18 (5  $\mu\text{m}$ , 150×4.6 mm); Column temperature: 20 °C; UV detection wavelength: 214 nm; Flow phase composition: mobile phase a ( phosphoric acid - acetonitrile - water : 0.5: 400: 600 ), mobile phase B ( acetonitrile ); Flow rate: 2.0 mL/ min; Amount of injection: 20  $\mu\text{l}$ : The linear gradient elution is performed by flow phase A and B according to table 1.

**Table 1.** Elution gradient

Time/min	A/%	B/%
0	100	0
25	100	0

55	15	85
70	15	85
75	100	0

The retention time of impurity B was approximately 1.1 times of the retention time of the control product, and the retention time of ibuprofen was close to 16 min. In the contrast solution B chromatography, the peak to valley ratio should not be less than 1.5; By injection of reference solution C 20 uL, the retention time of impurity j is approximately 2 times longer than that of the hub tamoxifen retention time, and the impurity n retention time is approximately 3 times of the hub tamoxifen retention time. the retention time of impurity a is approximately 9 times as long as the retention time of hub. injected into the control solution of a20 uL, the peak height of the main component chromatographic peak is about 20% of the full range. the sample solution is injected into the sample solution 20 uL, and the chromatographic diagram is recorded. if a known impurity A,B, J ,N are known in the chromatogram of the sample solution. The sum of the known impurity peaks shall not be greater than 2 times the peak area of the control solution a ( 0.2 % )<sup>[15-17]</sup>.

### 3.4 Determination of ibuprofen granules

**3.4.1 Solution preparation.** Preparation of test solution: Take the sample 10 bags as the appropriate amount ( approximately hub tamoxifen ), two, obtain the sample 1 is 0.01210 g, the sample 2 is 0.01240 g , place the 25 mL bottle with mobile phase to the scale of the test solution; Preparation of reference substance: Take two ibuprofen control samples in a 50 ml bottle, and get the m1 is 0.1286 g, m2 is 0.1271 g, and the flow phase contrast solution.

**3.4.2 Determination condition.** Column: C18 ( 2.6 um, 100×4.6 mm); Column temperature: 30°C; UV detection wavelength: 222 nm; Mobile phase composition: acetonitrile - 0.25mol/L ammonium dihydrogen phosphate - water ( mixed with ammonia solution to adjust pH to 7.0 ); Mobile phase ratio is 1000:284:1714; Flow rate: 1.0 mL / min; Amount of injection: 10 uL .

**3.4.3 Calculation of the results of the determination of the content.** This product contains ibuprofen for 90.0 % ~ 110.0 % of the labeled amount. calculation formula :

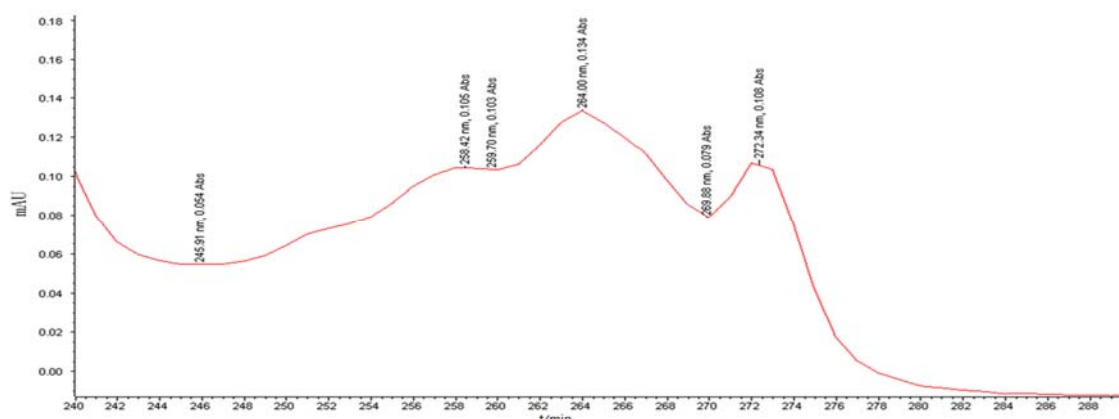
$$\frac{P}{B}\% = \frac{\bar{A} \times \bar{f} \times P \times n \times 20 \times \overline{W_{10or20}}}{m \times n \times 20 \times B} \times 100\% . \bar{A} : \text{The average peak area of the sample solution; } \bar{f} :$$

Comparison of sample volume / control solution peak area of reference substance; P: Control purity ( concentration ), this is known; n : The dilution multiple of the sample;  $\overline{W_{10or20}}$  : The sample sample takes the average weight of each bag of 10 or 20 bags; m : Sampling quantity for test articles; n : Dilution multiple of reference sample; B : Sample size, 0.2 g<sup>[18-19]</sup>.

## 4. Results

### 4.1 Identification of ibuprofen granules

he maximum absorption at the wavelength of 264 nm and 273 nm; Minimum absorption at 246 nm and 270 nm; There is a shoulder peak at 259 nm, as shown in Figure ure 1.



**Figure 1.** Ultraviolet absorption of ibuprofen granules

#### 4.2 Examination of ibuprofen granules

**4.2.1 Examination of ibuprofen granules.** This product is white or white granule; Fragrant air; Sweet taste.

**4.2.2 Examination of particle size of ibuprofen granules.** Particle size  $s = 5.012$ ; The sum of the particles that cannot be passed through no one sieve and the particles that can pass through the no 5 screen is 6 %.

**4.2.3 Examination of the difference of the amount of ibuprofen granules.** The results are as shown in table 2.

**Table 2.** The difference in loading of ibuprofen granules

Serial number	quality/g	Serial number	quality/g
1	1.0182	6	1.0012
2	0.9969	7	1.0501
3	1.0179	8	1.0139
4	0.9923	9	0.9911
5	1.0255	10	1.0788

Extent of limitation: 0.920 0~1.080 0 g.

**4.2.4 Examination of weight loss on drying detection of ibuprofen granules.** The results are as shown in table 3.

**Table 3.** Examination of weight loss on drying detection of ibuprofen granules

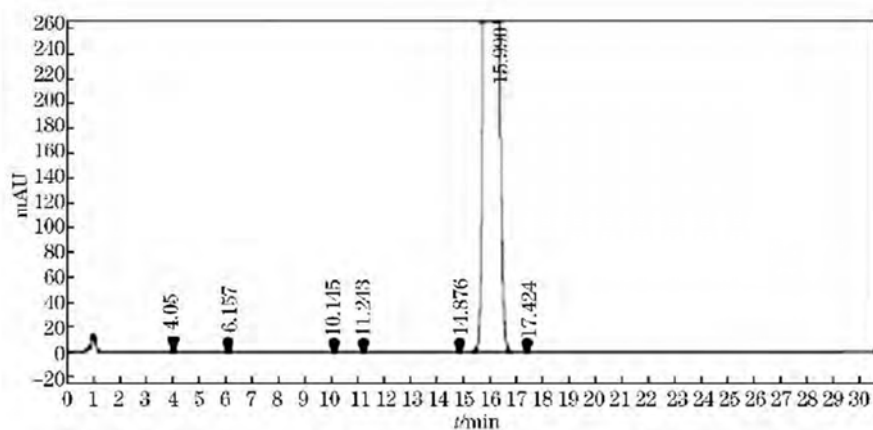
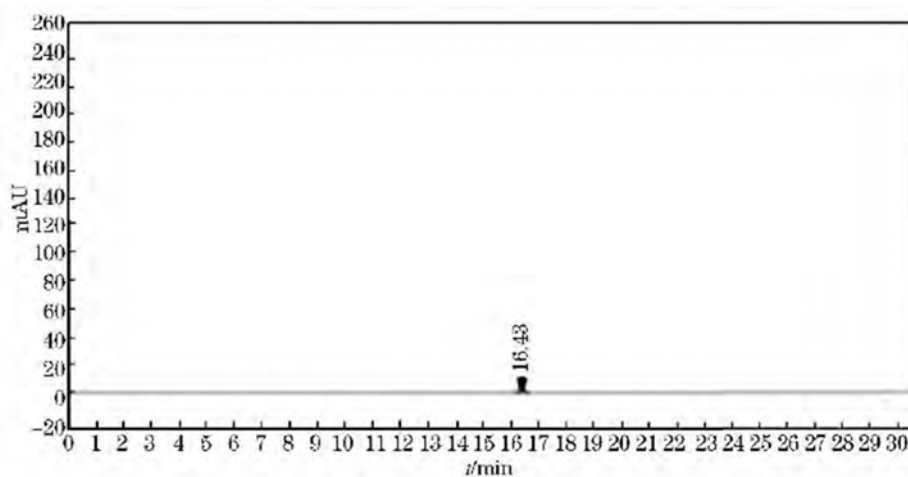
	frequency	drying time	Time of weighing	Test item 1/g	Test item 2/g
Weighing bottle	1	7:40~9:40	10:10	29.150 7	30.024 6
constant weight / g	2	10:11~12:11	12:41	29.150 9	30.024 5
Sample size / g				1.002 4	1.012 0
After drying	1	12:50~14:50	15:20	30.152 0	31.023 5
constant weight / g	2	15:21~17:21	17:51	30.152 1	31.023 4
Loss on drying /g				1.2	1.3

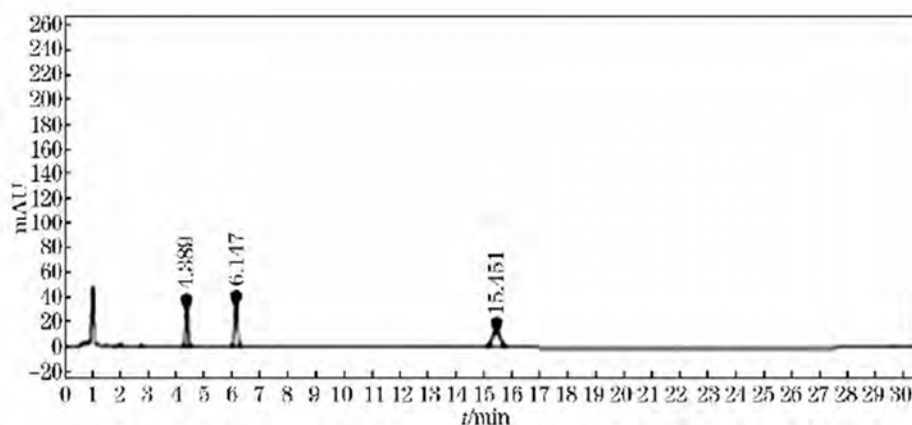
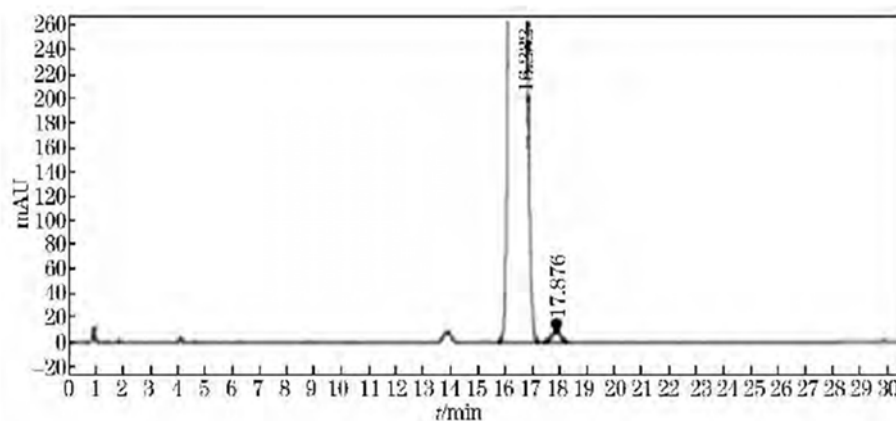
**4.2.5 Determination of the dissolution of ibuprofen granules.** The results are as shown in table 4.

**Table 4.** Determination of the dissolution of ibuprofen granules

Serial number	The absorbance	Elution/%	Serial number	The absorbance	Elution/%
1	0.909	91	4	0.938	94
2	0.916	92	5	0.941	95
3	0.925	93	6	0.954	96

4.3 Examination of the related substances of ibuprofen granules. The results are as shown in table 5.

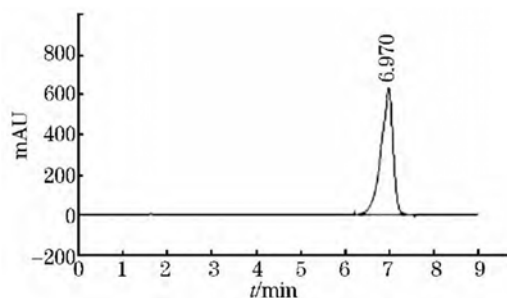
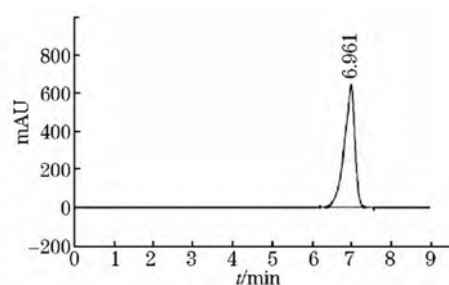
**Figure 2.**HPLC of sample solution**Figure 3.**HPLC Control solution A

**Figure 4.**HPLC Control solution B**Figure 5.**HPLC Control solution C**Table 5.**Examination of the related substances of ibuprofen granules

Project and standards	Calculation result	Project and standards	Calculation result
ImpurityA ( $\leq 0.15\%$ )	0.02%	ImpurityN ( $\leq 0.15\%$ )	0.01%
ImpurityB ( $\leq 0.15\%$ )	0.01%	Another impurity ( $\leq 0.05\%$ )	0.01%
ImpurityJ ( $\leq 0.15\%$ )	0.03%	All of impurity ( $\leq 0.2\%$ )	0.1%

#### 4.4 Determination of ibuprofen granules

##### 4.4.1 Content determination and determination of data

**Figure 6.** reference solution**Figure 7.** sample solution

4.4.2 Content determination results. The results are as shown in table6.

**Table 6.**Content determination results

	Retention time (t/min)	Peak area (mAU)	$f$ ( $1 \times 10^{-7}$ )	$\bar{f}$ ( $1 \times 10^{-7}$ )	$\frac{P}{B}$ (%)	$\frac{\bar{P}}{B}$ (%)
Reference solution1-1	7.087	12185.8	9.8635	10.0175	91.98	93.98
Reference solution1-2	7.019	12348.8				
Reference solution2-1	6.993	12249.5	10.0295	10.0175	95.97	93.98
Reference solution2-2	6.981	12067.1				
Sample solution1-1	6.970	11790.7	9.8635	10.0175	91.98	93.98
Sample solution1-2	6.961	11763.5				
Sample solution2-1	6.949	12256.1	10.0295	10.0175	95.97	93.98
Sample solution2-2	6.948	11876.4				

## 5. Conclusion

Through the total quality detection and the determination of effective components of ibuprofen granules, the conclusion is as follows: the appearance and smell of ibuprofen granules are in accordance with the standard characters. In the particle size, UV spectrophotometry, loading variance, loss on drying, dissolution test and related substances inspection, each detection sample is in accordance with the requirements of the standard. in the quality inspection, the effective ingredient of ibuprofen granules is Ibuprofen, and the content is 93. 98 %, conforming to the standard. in conclusion, the detection indexes of the detection of ibuprofen granules are in accordance with the standard and can be listed.

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