to about 1.38-fold, at % ratio.

When the pharmaceutically active ingredient is compound A, and fumaric acid is further added in addition to the fumarate compound of compound A as the material, the content of the reaction product in the liquid preparation of the present invention after treatment at 123°C in an autoclave is preferably not more than 1%, more preferably not more than 0.80% (e.g., not less than 0.02% and not more than 0.80%), further preferably not more than 0.70% (e.g., not less than 0.02% and not more than 0.70%), by the measurement at Rt:0.79 (Rt is a relative retention time when the elution time of compound A is 1). The increase ratio of the reaction product is preferably not more than about 6-fold, more preferably not more than about 5-fold, still more preferably not more than about 4.5-fold.

The percentage of the content (%) of the reaction product is the ratio ~~thereof~~ to the total peak area of the pharmaceutically active ingredient compound and an analog thereof (reaction product), ~~with~~ to the area on the chromatograph as 100%, which is detected by the HPLC method (high performance liquid chromatography method), and the increase rate is obtained by dividing the content (%) of the reaction product in the liquid preparation calculated after preservation by the content(%) of the reaction product in the liquid preparation calculated before preservation (content (%) of reaction product after preservation/content (%) of reaction product before preservation).

The content of the reaction product can be measured according to Experimental Examples 1-5, 8 and 10 to be mentioned later under the following HPLC test conditions.

[HPLC test conditions]

system: Waters 2690 Separation Module

detector: ultraviolet absorption spectrophotometer (measurement wavelength: 230 nm) (waters 2487 Dual λ Absorbance Detector)

manufactured by YAMATO SCIENTIFIC CO., LTD.", resistance value not less than 15.0 MΩcm) to give a total volume of 1000 mL, and the solution was diluted 2-fold. It was confirmed that the pH after the dilution was 6.8. When it was not 6.8, phosphoric acid (reagent special grade, Wako Pure Chemical Industries, Ltd.) or 0.1 mol/L sodium hydroxide solution (for volumetric analysis, Wako Pure Chemical Industries, Ltd.) was added to adjust the pH to 6.8.

The concentration gradient of the feed for the mobile lo phase was controlled by changing the mixing ratio of the mobile phase as follows.

[0171]

Table 17

time (min)	mobile phase A (%)	mobile phase B (%)
0 (injection)	100	0
10	100	0
30	50	50
40	0	100
45	0	100
45.1	100	0
55 (injection)	100	0

[0172]

In Comparative Example 7 and Example 13, the reaction product was measured before and after of the autoclave treatment for 3 hr and 6 hr. The results are shown in Table 18. An increase of the reaction product that increases by the addition of fumaric acid was suppressed by the addition of sodium chloride.