

## 1 Solifenacin Succinate Tablets

2 ソリフェナシンコハク酸塩錠

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4 Solifenacin Succinate Tablets contain not less than  
5 95.0% and not more than 105.0% of the labeled amount  
6 of solifenacin succinate ( $C_{23}H_{26}N_2O_2 \cdot C_4H_6O_4$ ; 480.55).

7 **Method of preparation** Prepare as directed under Tablets,  
8 with Solifenacin Succinate.

9 **Identification** To a quantity of powdered Solifenacin Suc-  
10 cinate Tablets, equivalent to 20 mg of solifenacin succinate  
11 ( $C_{23}H_{26}N_2O_2 \cdot C_4H_6O_4$ ), add 40 mL of methanol, shake thor-  
12 oughly, and filter through a membrane filter with a pore size  
13 not exceeding  $0.45 \mu\text{m}$ . Determine the absorption spectrum  
14 of the filtrate as directed under Ultraviolet-visible Spectro-  
15 photometry <2.24>: it exhibits maxima between 257 nm and  
16 261 nm, and between 263 nm and 267 nm.

17 **Purity** Related substances—To 10 tablets of Solifenacin  
18 Succinate Tablets add about 3V/5 mL of a mixture of water  
19 and acetonitrile (7:3), disintegrate the tablets by sonicating  
20 with occasional thorough shaking, and add a mixture of water  
21 and acetonitrile (7:3) to make exactly V mL so that each mL  
22 contains about 0.5 mg of solifenacin succinate  
23 ( $C_{23}H_{26}N_2O_2 \cdot C_4H_6O_4$ ). Filter this solution through a mem-  
24 brane filter with a pore size not exceeding  $0.45 \mu\text{m}$ . Discard  
25 the first 5 mL of the filtrate, and use the subsequent filtrate  
26 as the sample solution. Pipet 1 mL of the sample solution,  
27 add a mixture of water and acetonitrile (7:3) to make exactly  
28 100 mL, and use this solution as the standard solution. Per-  
29 form the test with exactly 10  $\mu\text{L}$  each of the sample solution  
30 and standard solution as directed under Liquid Chromatog-  
31 raphy <2.01> according to the conditions described below.  
32 Determine each peak area by the automatic integration  
33 method. Calculate the amount of each related substance and  
34 the total amount of related substances by the following equa-  
35 tion: the amount of the related substance TA, having the rel-  
36 ative retention time of about 0.5 to solifenacin, is not more  
37 than 0.3%, the amount of the related substance TB, having  
38 the relative retention time of about 0.8, is not more than 1.0%,  
39 the amount of each related substance other than the sub-  
40 stances mentioned above is not more than 0.2%, and the total  
41 amount of related substances is not more than 1.3%.

42 Amount (%) of each related substance =  $A_T/A_S$

43 Total amount (%) of related substances =  $\Sigma A_T/A_S$

44  $A_S$ : Peak area of solifenacin from the standard solution

45  $A_T$ : Peak area of each related substance from the sample  
46 solution

47  $\Sigma A_T$ : Total peak area of related substances from the sample  
48 solution

49 *Operating conditions*—

50 Detector, column, column temperature and mobile phase:  
51 Proceed as directed in the operating conditions in the Assay  
52 under Solifenacin Succinate.

53 Flow rate: Adjust so that the retention time of solifenacin  
54 is about 15 minutes.

55 Time span of measurement: About 2 times as long as the  
56 retention time of solifenacin, beginning after the solvent and  
57 succinic acid peaks.

58 *System suitability*—

59 System performance: Proceed as directed in the system  
60 suitability in the Assay.

61 Test for required detectability: To exactly 2.5 mL of the  
62 standard solution add a mixture of water and acetonitrile (7:3)  
63 to make exactly 50 mL. Confirm that the peak area of sol-  
64 ifenacin obtained with 10  $\mu\text{L}$  of this solution is equivalent to  
65 3.5 to 6.5% of that with 10  $\mu\text{L}$  of the standard solution.

66 System repeatability: When the test is repeated 6 times  
67 with 10  $\mu\text{L}$  of the standard solution under the above operating  
68 conditions, the relative standard deviation of the peak area of  
69 solifenacin is not more than 2.0%.

70 **Uniformity of dosage units** <6.02> Perform the test ac-  
71 cording to the following method: it meets the requirement of  
72 the Content uniformity test.

73 To 1 tablet of Solifenacin Succinate Tablets add about 8  
74 mL of a mixture of water and acetonitrile (7:3), disintegrate  
75 the tablet by sonicating with occasional thorough shaking,  
76 and add a mixture of water and acetonitrile (7:3) to make ex-  
77 actly 10 mL. Filter this solution through a membrane filter  
78 with a pore size not exceeding  $0.45 \mu\text{m}$ . Discard the first 5  
79 mL of the filtrate, and use the subsequent filtrate as the sam-  
80 ple solution. Separately, weigh accurately about 50 mg of  
81 Solifenacin Succinate RS, and dissolve in a mixture of water  
82 and acetonitrile (7:3) to make exactly V mL so that each mL  
83 contains about 1/10 of the labeled amount of solifenacin suc-  
84 cinate ( $C_{23}H_{26}N_2O_2 \cdot C_4H_6O_4$ ), and use this solution as the  
85 standard solution. Perform the test with exactly 10  $\mu\text{L}$  each  
86 of the sample solution and standard solution as directed under  
87 Liquid Chromatography <2.01> according to the conditions  
88 described below. Determine the peak areas,  $A_T$  and  $A_S$ , of sol-  
89 ifenacin in each solution.

90 Amount (mg) of solifenacin succinate ( $C_{23}H_{26}N_2O_2 \cdot C_4H_6O_4$ )  
91 =  $M_S/V \times A_T/A_S \times 10$

92  $M_S$ : Amount (mg) of Solifenacin Succinate RS taken

93 *Operating conditions*—

94 Detector, column, column temperature and mobile phase:  
95 Proceed as directed in the operating conditions in the Assay  
96 under Solifenacin Succinate.

97 Flow rate: Adjust so that the retention time of solifenacin  
98 is about 15 minutes.

99 *System suitability*—

100 System performance: Proceed as directed in the system  
101 suitability in the Assay.

102 System repeatability: When the test is repeated 6 times  
103 with 10  $\mu\text{L}$  of the standard solution under the above operating  
104 conditions, the relative standard deviation of the peak area of  
105 solifenacin is not more than 2.0%.

106 **Dissolution** <6.10> When the test is performed at 50 revo-  
107 lutions per minute according to the Paddle method, using 900  
108 mL of water as the dissolution medium, the dissolution rate  
109 in 30 minutes of Solifenacin Succinate Tablets is not less than  
110 80%.

111 Start the test with 1 tablet of Solifenacin Succinate Tablets,  
112 withdraw not less than 10 mL of the medium at the specified  
113 minute after starting the test, and filter through a membrane  
114 filter with a pore size not exceeding 0.45  $\mu\text{m}$ . Discard not less  
115 than 5 mL of the first filtrate, pipet 3.5 mL of the subsequent  
116 filtrate, add exactly 1.5 mL of acetonitrile, shake thoroughly,  
117 and use this solution as the sample solution. Separately,  
118 weigh accurately about 28 mg of Solifenacin Succinate RS,  
119 and dissolve in a mixture of water and acetonitrile (7:3) to  
120 make exactly 100 mL. Pipet  $V$  mL of this solution containing  
121 solifenacin succinate ( $\text{C}_{23}\text{H}_{26}\text{N}_2\text{O}_2\cdot\text{C}_4\text{H}_6\text{O}_4$ ) equivalent to  
122 7/25 of the labeled amount, and add water to make exactly  
123 250 mL. Pipet 3.5 mL of the solution, add exactly 1.5 mL of  
124 acetonitrile, shake thoroughly, and use this solution as the  
125 standard solution. Perform the test with exactly 50  $\mu\text{L}$  each  
126 of the sample solution and standard solution as directed under  
127 Liquid Chromatography <2.01> according to the conditions  
128 described below. Determine the peak areas,  $A_T$  and  $A_S$ , of sol-  
129 ifenacin in each solution.

130 Dissolution rate (%) with respect to the labeled amount of  
131 solifenacin succinate ( $\text{C}_{23}\text{H}_{26}\text{N}_2\text{O}_2\cdot\text{C}_4\text{H}_6\text{O}_4$ )  
132  $=M_S \times A_T/A_S \times V \times 1/C \times 18/5$

133  $M_S$ : Amount (mg) of Solifenacin Succinate RS taken

134  $C$ : Labeled amount (%) of solifenacin succinate  
135 ( $\text{C}_{23}\text{H}_{26}\text{N}_2\text{O}_2\cdot\text{C}_4\text{H}_6\text{O}_4$ ) in 1 tablet

136 *Operating conditions*—

137 Detector, column and column temperature: Proceed as di-  
138 rected in the operating conditions in the Assay under Solifen-  
139 acin Succinate.

140 Mobile phase: Dissolve 8.7 g of dipotassium hydrogen  
141 phosphate in water to make 1000 mL, and adjust to pH 6.0  
142 with phosphoric acid. To 650 mL of this solution add 350 mL  
143 of acetonitrile for liquid chromatography.

144 Flow rate: Adjust so that the retention time of solifenacin  
145 is about 9 minutes.

146 *System suitability*—

147 System performance: To 10 mg of Solifenacin Succinate  
148 RS, add 1 mL of hydrogen peroxide (30) and 5 mL of sodium

149 hydroxide solution (43 in 10000), and then add 15 mL of a  
150 mixture of water and acetonitrile (7:3). Stir this solution for  
151 10 minutes, and use as the related substance TB solution.  
152 Separately, weigh 5 mg of Solifenacin Succinate RS, add 0.1  
153 mol/L hydrochloric acid TS to make 10 mL. To 1 mL of this  
154 solution, add 1 mL of the related substance TB solution, and  
155 add a mixture of water and acetonitrile (7:3) to make 100 mL.  
156 When the procedure is run with 50  $\mu\text{L}$  of this solution under  
157 the above operating conditions, the related substance TB and  
158 solifenacin are eluted in this order with the resolution be-  
159 tween these peaks being not less than 3.

160 System repeatability: When the test is repeated 6 times  
161 with 50  $\mu\text{L}$  of the standard solution under the above operating  
162 conditions, the relative standard deviation of the peak area of  
163 solifenacin is not more than 2.0%.

164 **Assay** To 20 tablets of Solifenacin Succinate Tablets add  
165 about 3V/5 mL of a mixture of water and acetonitrile (7:3),  
166 disintegrate the tablets by sonicating with occasional thor-  
167 ough shaking, and add a mixture of water and acetonitrile  
168 (7:3) to make exactly  $V$  mL so that each mL contains about  
169 0.5 mg of solifenacin succinate ( $\text{C}_{23}\text{H}_{26}\text{N}_2\text{O}_2\cdot\text{C}_4\text{H}_6\text{O}_4$ ). Filter  
170 this solution through a membrane filter with a pore size not  
171 exceeding 0.45  $\mu\text{m}$ . Discard the first 5 mL of the filtrate, and  
172 use the subsequent filtrate as the sample solution. Separately,  
173 weigh accurately about 50 mg of Solifenacin Succinate RS,  
174 and dissolve in a mixture of water and acetonitrile (7:3) to  
175 make exactly 100 mL, and use this solution as the standard  
176 solution. Perform the test with exactly 10  $\mu\text{L}$  each of the sam-  
177 ple solution and standard solution as directed under Liquid  
178 Chromatography <2.01> according to the conditions de-  
179 scribed below. Determine the peak areas,  $A_T$  and  $A_S$ , of sol-  
180 ifenacin in each solution.

181 Amount (mg) of solifenacin succinate ( $\text{C}_{23}\text{H}_{26}\text{N}_2\text{O}_2\cdot\text{C}_4\text{H}_6\text{O}_4$ )  
182 in 1 tablet

183  $=M_S \times A_T/A_S \times V \times 1/2000$

184  $M_S$ : Amount (mg) of Solifenacin Succinate RS taken

185 *Operating conditions*—

186 Detector, column, column temperature and mobile phase:  
187 Proceed as directed in the operating conditions in the Assay  
188 under Solifenacin Succinate.

189 Flow rate: Adjust so that the retention time of solifenacin  
190 is about 15 minutes.

191 *System suitability*—

192 System performance: To 10 mg of Solifenacin Succinate  
193 RS, add 1 mL of hydrogen peroxide (30) and 5 mL of sodium  
194 hydroxide solution (43 in 10000), and then add 15 mL of a  
195 mixture of water and acetonitrile (7:3). Stir this solution for  
196 10 minutes, and use as the related substance TB solution.  
197 Separately, weigh 5 mg of Solifenacin Succinate RS, add 0.1  
198 mol/L hydrochloric acid TS to make 10 mL. To 1 mL of this

199 solution, add 1 mL of the related substance TB solution, and  
 200 add a mixture of water and acetonitrile (7:3) to make 100 mL.  
 201 When the procedure is run with 10  $\mu$ L of this solution under  
 202 the above operating conditions, the related substance TB and  
 203 solifenacin are eluted in this order with the resolution be-  
 204 tween these peaks being not less than 3.

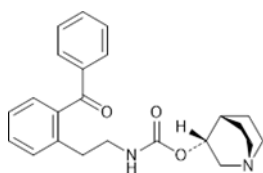
205 System repeatability: When the test is repeated 6 times  
 206 with 10  $\mu$ L of the standard solution under the above operating  
 207 conditions, the relative standard deviation of the peak area of  
 208 solifenacin is not more than 1.0%.

209 **Containers and storage** Containers—Tight containers.

210 **Others**

211 Related substance TA:

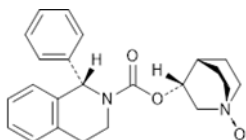
212 (3*R*)-1-Azabicyclo[2.2.2]octan-3-yl[2-(2-  
 213 benzoylphenyl)ethyl]carbamate



214

215 Related substance TB:

216 (3*R*)-3-[[*(1S)*-1-Phenyl-3,4-dihydroisoquinoline-2(*1H*)-  
 217 carbonyl]oxy]-1-azabicyclo[2.2.2]octane 1-oxide



218

219 **Add the following to 9.01 Reference**  
 220 **Standards (1):**

221 Solifenacin Succinate RS

222