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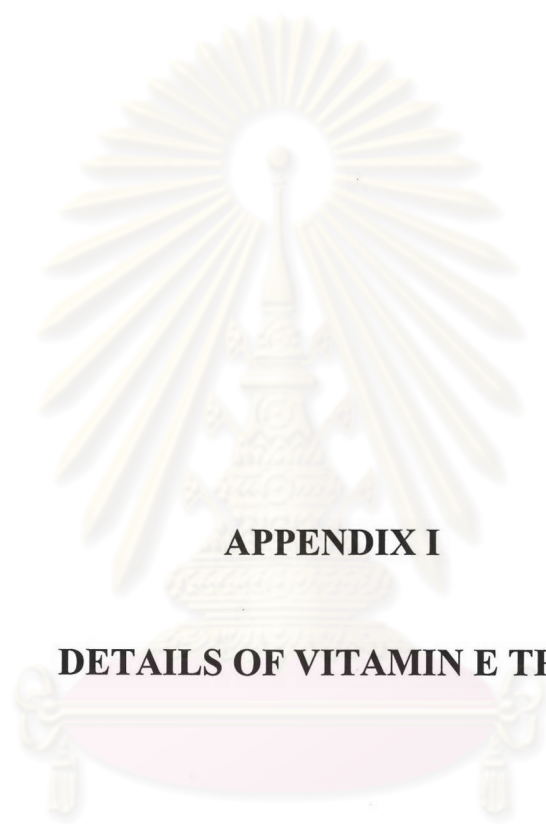
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APPENDICES

ศูนย์วิทยทรัพยากร
จุฬาลงกรณ์มหาวิทยาลัย



APPENDIX I

DETAILS OF VITAMIN E TPGS

ศูนย์วิทยทรัพยากร
จุฬาลงกรณ์มหาวิทยาลัย

source of vitamin E for individuals who have difficulties absorbing fat soluble vitamin E forms.

- Because of its chemical functionality and water-soluble characteristics, VE TPGS can emulsify lipophilic (fat-soluble) drugs.
- VE TPGS does not require the action of bile salts or pancreatic enzymes for absorption into the intestinal wall. Therefore, it provides a source of vitamin E for individuals with specific disease in which liver or pancreatic function may be impaired.
- VE TPGS may enhance the bioavailability of fat soluble drugs that are otherwise difficult to absorb, especially in individual with compromised liver or pancreatic function.

Typical properties

| | |
|---------------------------|----------------------|
| Molecular weight | 1,513 |
| Physical form | Waxy solid |
| Appearance | White to light brown |
| Acid value | 1.5 |
| Specific gravity at 45 °C | 1.06 |
| Melting point °C (°F) | 37-41 (72-106) |
| Solubility in water | Missible in all part |
| HLB value | ~13 |

Stability

- VE TPGS is a highly stable form of vitamin E that does not degrade if exposed to oxygen, heat, light, or oxidizing agents normally found in nutrition supplements. It is unstable to alkali. VE TPGS should be stored in a sealed container in a dry location.
- Heat stability of VE TPGS was determined by differential scanning calorimetry in ambient air. VE TPGS was found to be stable when heated to 125 °C (257 °F) for 1 h, conditions that exceed the temperature and time required for heat sterilization. VE TPGS was also found to be stable repetitive heat/cool/reheat cycle.

Solutions

- VE TPGS is commonly used to form a 20% aqueous solution that can be used as a form of vitamin E supplement.

Esterification

- VE TPGS can be melt-blended with a lipophilic drug and emulsified in water. This technique can be used to emulsify a drug prior to use for applications such as a topical lotion or an oral suspension.



APPENDIX II

**CUMULATIVE AMOUNT OF TMZ-HE PERMEATED FROM
MICROEMULSION FORMULATIONS AND CONTROL NEAT
OIL SOLUTION**

ศูนย์วิทยทรัพยากร
จุฬาลงกรณ์มหาวิทยาลัย

Table 16. Cumulative amount of TMZ-HE permeated from ME 1 through silicone membrane

| Time (h) | Cumulative amount permeated (nmol/cm ²) | | | Average | s.d. |
|----------|--|---------|---------|---------|--------|
| | 1 | 2 | 3 | | |
| 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| 0.50 | 71.23 | 57.69 | 64.69 | 64.54 | 6.77 |
| 1.00 | 112.32 | 104.77 | 114.46 | 110.52 | 5.09 |
| 1.50 | 156.76 | 146.00 | 158.62 | 153.79 | 6.82 |
| 2.00 | 202.39 | 188.23 | 206.36 | 198.99 | 9.53 |
| 2.50 | 250.95 | 233.12 | 248.86 | 244.31 | 9.75 |
| 3.00 | 291.12 | 267.66 | 296.66 | 285.15 | 15.40 |
| 3.50 | 336.01 | 312.02 | 335.47 | 327.83 | 13.70 |
| 4.00 | 383.22 | 347.43 | 377.84 | 369.50 | 19.30 |
| 4.50 | 407.37 | 379.23 | 419.93 | 402.18 | 20.84 |
| 5.00 | 449.62 | 418.27 | 447.12 | 438.34 | 17.42 |
| 6.00 | 529.60 | 477.36 | 521.57 | 509.51 | 28.13 |
| 7.00 | 594.79 | 538.78 | 601.34 | 578.30 | 34.38 |
| 8.00 | 680.13 | 584.63 | 647.69 | 637.48 | 48.56 |
| 21.00 | 1221.49 | 996.13 | 1205.28 | 1140.97 | 125.70 |
| 23.00 | 1285.77 | 1030.27 | 1257.90 | 1191.31 | 140.16 |
| 24.00 | 1291.77 | 1063.97 | 1302.70 | 1219.48 | 134.79 |

Table 17. Cumulative amount of TMZ-HE permeated from ME 2 through silicone membrane

| Time (h) | Cumulative amount permeated (nmol/cm ²) | | | Average | s.d. |
|----------|--|---------|---------|---------|-------|
| | 1 | 2 | 3 | | |
| 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| 0.50 | 51.81 | 58.56 | 62.62 | 57.67 | 5.46 |
| 1.00 | 110.06 | 107.32 | 106.09 | 107.82 | 2.03 |
| 1.50 | 148.10 | 148.92 | 145.77 | 147.60 | 1.63 |
| 2.00 | 177.87 | 186.73 | 199.77 | 188.13 | 11.01 |
| 2.50 | 232.47 | 228.78 | 235.94 | 232.39 | 3.58 |
| 3.00 | 266.87 | 260.92 | 277.93 | 268.57 | 8.63 |
| 3.50 | 307.54 | 291.23 | 267.97 | 288.91 | 19.89 |
| 4.00 | 339.78 | 328.02 | 349.85 | 339.22 | 10.92 |
| 4.50 | 369.00 | 360.43 | 385.77 | 371.73 | 12.89 |
| 5.00 | 391.24 | 389.09 | 411.95 | 397.43 | 12.62 |
| 6.00 | 453.42 | 434.86 | 466.73 | 451.67 | 16.01 |
| 7.00 | 507.92 | 486.57 | 514.45 | 502.98 | 14.58 |
| 8.00 | 548.30 | 534.73 | 561.82 | 548.28 | 13.55 |
| 21.00 | 970.91 | 978.77 | 965.14 | 971.61 | 6.84 |
| 23.00 | 1059.98 | 1043.84 | 1021.37 | 1041.73 | 19.39 |
| 24.00 | 1056.33 | 1066.12 | 1048.80 | 1057.08 | 8.68 |

Table 18. Cumulative amount of TMZ-HE permeated from ME 3 through silicone membrane

| Time (h) | Cumulative amount permeated (nmol/cm ²) | | | Average | s.d. |
|----------|---|---------|---------|---------|-------|
| | 1 | 2 | 3 | | |
| 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| 0.50 | 85.65 | 76.39 | 84.46 | 82.16 | 5.04 |
| 1.00 | 164.15 | 140.67 | 152.30 | 152.37 | 11.74 |
| 1.50 | 227.86 | 200.02 | 212.78 | 213.55 | 13.94 |
| 2.00 | 291.19 | 269.55 | 273.71 | 278.15 | 11.48 |
| 2.50 | 301.28 | 327.41 | 336.12 | 321.60 | 18.13 |
| 3.00 | 359.78 | 378.26 | 378.66 | 372.23 | 10.79 |
| 3.50 | 367.18 | 431.80 | 426.38 | 408.46 | 35.85 |
| 4.00 | 448.12 | 477.50 | 477.90 | 467.84 | 17.08 |
| 4.50 | 513.86 | 532.21 | 540.41 | 528.82 | 13.59 |
| 5.00 | 563.57 | 581.62 | 581.23 | 575.47 | 10.31 |
| 6.00 | 658.09 | 669.75 | 667.27 | 665.04 | 6.14 |
| 7.00 | 729.86 | 745.33 | 731.42 | 735.53 | 8.52 |
| 8.00 | 831.48 | 828.82 | 817.25 | 825.85 | 7.57 |
| 21.00 | 1461.37 | 1322.60 | 1308.89 | 1364.28 | 84.36 |
| 23.00 | 1548.67 | 1397.64 | 1393.83 | 1446.72 | 88.32 |
| 24.00 | 1581.79 | 1386.97 | 1463.87 | 1477.54 | 98.13 |

Table 19. Cumulative amount of TMZ-HE permeated from ME 4 through silicone membrane

| Time (h) | Cumulative amount permeated (nmol/cm ²) | | | Average | s.d. |
|----------|---|---------|--------|---------|--------|
| | 1 | 2 | 3 | | |
| 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| 0.50 | 93.78 | 121.24 | 144.10 | 119.70 | 25.20 |
| 1.00 | 194.93 | 232.79 | 223.56 | 217.09 | 19.74 |
| 1.50 | 303.21 | 343.56 | 338.58 | 328.45 | 22.00 |
| 2.00 | 408.93 | 453.61 | 429.27 | 430.60 | 22.37 |
| 2.50 | 499.78 | 542.82 | 429.27 | 490.62 | 57.33 |
| 3.00 | 594.08 | 651.93 | 429.27 | 558.42 | 115.53 |
| 3.50 | 678.50 | 779.51 | 429.27 | 629.09 | 180.27 |
| 4.00 | 736.64 | 872.93 | 429.27 | 679.61 | 227.26 |
| 4.50 | 824.12 | 970.30 | 429.27 | 741.23 | 279.88 |
| 5.00 | 887.25 | 1028.98 | 429.27 | 781.83 | 313.45 |
| 6.00 | 995.10 | 1178.52 | 429.27 | 867.63 | 390.55 |
| 7.00 | 1092.98 | 1330.11 | 429.27 | 950.79 | 466.95 |
| 8.00 | 1179.36 | 1459.72 | 429.27 | 1022.78 | 532.77 |
| 21.00 | 1746.24 | 2030.44 | 429.27 | 1401.98 | 854.30 |
| 23.00 | 1843.24 | 2122.22 | 429.27 | 1464.91 | 907.67 |
| 24.00 | 1919.15 | 2064.02 | 429.27 | 1470.81 | 904.91 |

Table 20. Cumulative amount of TMZ-HE permeated from ME 5 through silicone membrane

| Time (h) | Cumulative amount permeated (nmol/cm ²) | | | Average | s.d. |
|----------|---|---------|---------|---------|--------|
| | 1 | 2 | 3 | | |
| 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| 0.50 | 189.48 | 169.92 | 185.42 | 181.61 | 10.32 |
| 1.00 | 376.46 | 349.78 | 391.29 | 372.51 | 21.03 |
| 1.50 | 556.15 | 535.90 | 584.44 | 558.83 | 24.38 |
| 2.00 | 733.69 | 711.33 | 763.09 | 736.04 | 25.96 |
| 2.50 | 900.22 | 883.24 | 908.75 | 897.40 | 12.99 |
| 3.00 | 1055.43 | 1069.99 | 1076.73 | 1067.38 | 10.89 |
| 3.50 | 1192.91 | 1196.71 | 1220.27 | 1203.29 | 14.82 |
| 4.00 | 1347.81 | 1354.76 | 1367.81 | 1356.79 | 10.15 |
| 4.50 | 1440.53 | 1454.26 | 1464.63 | 1453.14 | 12.09 |
| 5.00 | 1575.80 | 1521.77 | 1526.97 | 1541.51 | 29.81 |
| 6.00 | 1719.87 | 1757.56 | 1715.12 | 1730.85 | 23.25 |
| 7.00 | 1934.09 | 1920.47 | 1948.08 | 1934.22 | 13.81 |
| 8.00 | 2009.89 | 2135.12 | 2125.11 | 2090.04 | 69.59 |
| 21.00 | 2876.82 | 3028.14 | 3075.13 | 2993.36 | 103.63 |
| 23.00 | 2919.00 | 3081.81 | 3161.70 | 3054.17 | 123.69 |
| 24.00 | 3045.12 | 3065.93 | 3167.91 | 3092.99 | 65.72 |

Table 21. Cumulative amount of TMZ-HE permeated from ME 3 through hairless mice skin

| Time (h) | Cumulative amount permeated (nmol/cm ²) | | | | | | Average | s.d. |
|----------|---|---------|---------|---------|---------|---------|---------|--------|
| | 1 | 2 | 3 | 4 | 5 | 6 | | |
| 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| 1.00 | 12.89 | 15.31 | 10.49 | 12.43 | 10.04 | 14.00 | 12.53 | 2.02 |
| 2.00 | 52.47 | 79.56 | 48.77 | 55.64 | 87.44 | 53.87 | 62.96 | 16.26 |
| 4.00 | 128.79 | 171.01 | 122.82 | 139.59 | 191.55 | 131.23 | 147.50 | 27.49 |
| 6.00 | 241.30 | 300.45 | 231.40 | 261.96 | 325.39 | 247.01 | 267.92 | 37.08 |
| 8.00 | 359.37 | 457.95 | 459.75 | 421.57 | 360.39 | 361.49 | 403.42 | 49.04 |
| 15.00 | 884.13 | 1112.77 | 854.23 | 1033.91 | 1109.97 | 921.86 | 986.14 | 114.53 |
| 20.00 | 1354.56 | 1729.96 | 1296.99 | 1529.60 | 1633.12 | 1424.53 | 1494.79 | 166.96 |
| 24.00 | 1561.37 | 2085.21 | 1740.94 | 1788.62 | 2040.06 | 1820.65 | 1839.47 | 195.25 |

Table 22. Cumulative amount of TMZ-HE permeated from neat OA through hairless mice skin

| Time (h) | Cumulative amount permeated (nmol/cm ²) | | | | Average | s.d. |
|----------|---|--------|--------|--------|---------|--------|
| | 1 | 2 | 3 | 4 | | |
| 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| 1.00 | 7.83 | 7.11 | 8.10 | 7.98 | 7.76 | 0.44 |
| 2.00 | 8.89 | 13.32 | 8.71 | 9.15 | 10.02 | 2.21 |
| 4.00 | 19.84 | 38.82 | 13.25 | 17.75 | 22.41 | 11.28 |
| 6.00 | 35.42 | 81.82 | 27.16 | 31.60 | 44.00 | 25.44 |
| 8.00 | 52.74 | 123.54 | 42.59 | 48.24 | 66.78 | 38.07 |
| 15.00 | 128.83 | 265.36 | 110.46 | 110.32 | 153.74 | 74.92 |
| 20.00 | 185.95 | 372.24 | 140.96 | 154.95 | 213.53 | 107.47 |
| 24.00 | 226.05 | 420.35 | 160.31 | 175.95 | 245.67 | 119.79 |

Table 23. Cumulative amount of TMZ-HE permeated from ME 5 through hairless mice skin

| Time (h) | Cumulative amount permeated (nmol/cm ²) | | | | | | Average | s.d. |
|----------|---|---------|---------|---------|---------|---------|---------|--------|
| | 1 | 2 | 3 | 4 | 5 | 6 | | |
| 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| 1.00 | 22.18 | 22.62 | 32.21 | 33.57 | 31.60 | 26.48 | 28.11 | 5.04 |
| 2.00 | 71.11 | 79.79 | 102.52 | 101.02 | 95.21 | 80.13 | 88.30 | 13.01 |
| 4.00 | 211.29 | 236.92 | 269.68 | 283.06 | 263.03 | 228.43 | 248.73 | 27.48 |
| 6.00 | 370.96 | 442.82 | 496.48 | 496.90 | 472.32 | 403.77 | 447.21 | 51.47 |
| 8.00 | 568.42 | 650.97 | 709.16 | 724.51 | 703.86 | 595.28 | 658.70 | 65.04 |
| 15.00 | 1221.56 | 1418.94 | 1469.38 | 1496.50 | 1488.37 | 1319.98 | 1402.46 | 110.00 |
| 20.00 | 1684.41 | 2098.50 | 1990.38 | 2083.45 | 2099.31 | 1830.99 | 1964.51 | 171.59 |
| 24.00 | 2159.53 | 2392.14 | 2420.40 | 2420.85 | 2541.07 | 2188.55 | 2353.76 | 148.67 |

Table 24. Cumulative amount of TMZ-HE permeated from neat IPM through hairless mice skin

| Time (h) | Cumulative amount permeated (nmol/cm ²) | | | | Average | s.d. |
|----------|---|--------|---------|---------|---------|--------|
| | 1 | 2 | 3 | 4 | | |
| 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| 1.00 | 23.15 | 24.65 | 25.14 | 17.23 | 22.55 | 3.64 |
| 2.00 | 58.24 | 50.44 | 57.89 | 40.43 | 51.75 | 8.36 |
| 4.00 | 157.06 | 102.79 | 127.09 | 113.26 | 125.05 | 23.55 |
| 6.00 | 226.68 | 179.39 | 228.01 | 208.48 | 210.64 | 22.66 |
| 8.00 | 334.90 | 249.02 | 336.40 | 347.74 | 317.01 | 45.69 |
| 15.00 | 687.05 | 523.39 | 703.81 | 724.96 | 659.80 | 92.25 |
| 20.00 | 930.27 | 745.56 | 956.81 | 1021.65 | 913.57 | 118.40 |
| 24.00 | 1183.81 | 915.11 | 1182.03 | 1260.68 | 1135.41 | 151.37 |

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