





Summary of clinical science conducted on Actazin®, other kiwifruit powders and whole green kiwifruit.

| Product              | Daily dose | Intervention<br>period | RCT | Population                |                             |          |     | Clinical Endpoint Key Results |                    |                                 |                       |
|----------------------|------------|------------------------|-----|---------------------------|-----------------------------|----------|-----|-------------------------------|--------------------|---------------------------------|-----------------------|
|                      |            |                        |     | Healthy - no constipation | Healthy - mild constipation | IBS-C/FC | n   | Stool Form                    | Stool<br>frequency | Symptoms<br>/ Ease /<br>Comfort | Ref                   |
| Actazin®             | 600 mg     | 4 weeks                | √   | √                         |                             |          | 19  | 0                             | •                  | 0                               | [1]                   |
|                      | 600 mg     | 4 weeks                | √   |                           |                             | √        | 9   | 0                             |                    | 0                               |                       |
|                      | 2,400 mg   | 4 weeks                | √   | √                         |                             |          | 19  | 0                             |                    | 0                               |                       |
| Actazin®             | 600 mg     | 4 weeks                | √   |                           | √                           |          | 43  |                               |                    |                                 | [2]                   |
| Kiwifruit<br>extract | 1,000 mg   | 3 weeks                | √   |                           | √                           |          | 32  | 0                             | •                  | •                               | [3]                   |
| Kiwifruit<br>powder  | 2,160 mg   | 1 week                 | √   |                           | √                           |          | 28  | •                             | •                  | •                               | [4]                   |
| Kiwifruit<br>powder  | 6 capsules | 4 weeks                | х   |                           | √                           |          | 41  | •                             | •                  | •                               | [5]                   |
| Kiwifruit<br>powder  | 3,000 mg   | 6 weeks                | √   |                           | <b>V</b>                    |          | 11  | 0                             | 0                  | •                               | [6]                   |
| Kiwifruit<br>powder  | 5,500 mg   | 4 weeks                | √   |                           | <b>V</b>                    |          | 39  | •                             | •                  | •                               | [7]                   |
| Whole<br>kiwifruit   | 2 fruit    | 2 weeks                | √   | √                         |                             |          | 11  | •                             | •                  | 0                               | [8]                   |
| Whole<br>kiwifruit   | 2 fruit    | 4 weeks                | √   |                           |                             | V        | 121 | •                             | •                  | •                               | [9, 10, 11<br>12, 16] |
| Whole<br>kiwifruit   | 2 fruit    | 4 weeks                | Х   |                           |                             | √        | 79  | •                             | •                  | •                               | [13]                  |
| Whole<br>kiwifruit   | 2-3 fruit  | 6 weeks                | X   | √                         |                             |          | 48  | •                             | •                  | •                               | [14]                  |
| Whole<br>kiwifruit   | 2-3 fruit  | 3 weeks                | x   | √                         |                             |          | 38  | •                             | •                  | •                               | [14]                  |
| Whole<br>kiwifruit   | 4 fruit    | 3 days                 | √   | √                         |                             |          | 14  | •                             | •                  | 0                               | [15]                  |

= significant improvement

= non-significant improvement

= no change, positive result

 $\bigcirc$  = no change

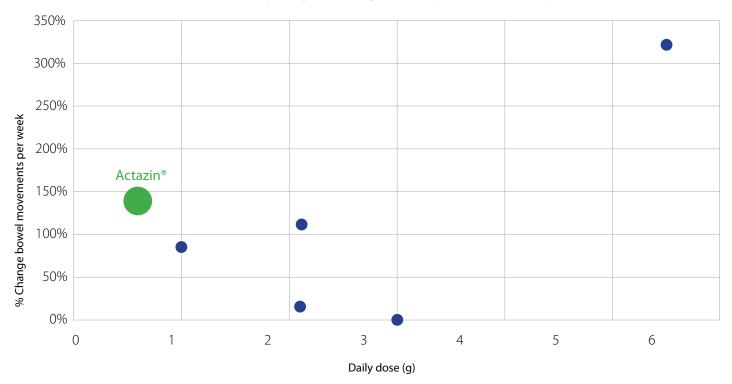
RCT = randomised controlled trial

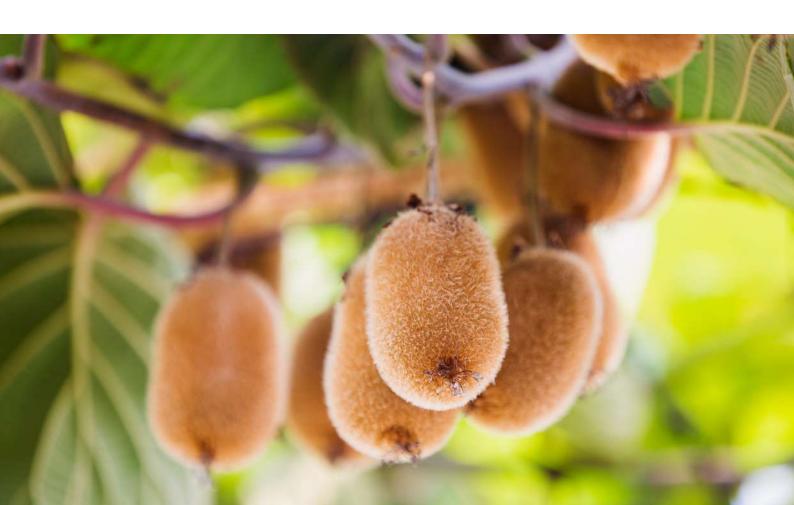


Actazin® at a low dose of 600 mg significantly increases the number of bowel movements per week in constipated individuals with superior effects compared to other kiwifruit powders at higher doses.

A 600 mg dose of Actazin provides the same benefits to bowel regularity as 2 or more whole green kiwifruit.

## Increase in stool frequency following consumption of kiwifruit powders





## Clinical studies details

|                                     | Dose and Intervention   | Study design,  | Clinical Endpoint Key Results   |   |  |    |  |
|-------------------------------------|---|--|---|---|--|----|--|
| Product                             | period  | population   | Stool Form (Bristol<br>Stool Scale (BSS))   | BM number/ frequency  | equency Symptoms / Ease / Comfort  |    |  |
|                                     |   | Randomised, double-<br>blind, placebo-controlled,<br>crossover (RCT)   | No significant changes  | 2,400 mg Significant increase in weekly BM + 0.77 in whole group (p = 0.014 vs washout) + 1.47 in responders (p < 0.001 vs washout) | No significant changes*,<br>already healthy  |    |  |
| Actazin®                            | 600mg or 2,400 mg/day;<br>4 weeks each, 2-week<br>washout   | Healthy (no constipation),<br>n = 19   | - did not induce looser<br>stools in already healthy<br>people                                    | 600 mg Near-significant increase in weekly BM for whole group +0.56 (p = 0.06 vs washout)   |  | [1 |  |
|                                     |   | Functionally constipated,<br>n = 9<br>(*NB: not sufficiently   | No significant changes*   | Significant increase in weekly BM in responders +1.19 (p = 0.005 vs washout)  Non-significant increase with 600 mg in responders:   | No significant changes*  | _  |  |
|                                     |   | powered due to recruitment issues)   | 140 significant changes   | weekly change = +1.82<br>(p = 0.087)  | 140 significant changes  |    |  |
| Actazin <sup>®</sup>                | 600 mg/day;<br>4 weeks each   | Multi-centered,<br>randomized, double-<br>blind, placebo-controlled,<br>parallel study (RCT)<br>Healthy with constipation, | Significantly softer stools,<br>BSS +0.38 (day 14, p<br>< 0.05 vs placebo and<br>baseline)        | Significant increase in<br>weekly CSBM<br>+1.44 (at endpoint, p < 0.001<br>vs baseline)   | Significant improvements in abdominal, rectal and stool symptoms and quality of life scores (p < 0.01 vs baseline) | [2 |  |
|                                     |   | n = 43   |   |   | (p < 0.01 vs baseline)   |    |  |
| Kiwifruit powder<br>(water extract) | Freeze-dried water extract<br>of green kiwifruit skin and<br>flesh (Digesten), 1,000<br>mg /day;<br>3-weeks, 3-9 week | Randomised, double-<br>blind, placebo-controlled,<br>crossover (RCT)<br>Healthy, constipated,                              | No significant changes<br>in BSS  | Significant increase in<br>weekly BM +2.12 (p < 0.05 vs<br>pre-trial frequency)   | Significant improvement<br>in gastrointestinal<br>symptoms score   | [3 |  |
|                                     | washout   | n = 32<br>Randomised, double-  |   |   |  |    |  |
| Kiwifruit powder<br>(freeze-dried)  | Freeze-dried green<br>kiwifruit powder<br>(Zyactinase), 2,160 mg<br>/ day<br>1-week                                   | blind, placebo-controlled,<br>parallel (RCT)  Healthy, constipated,<br>n = 28  | Significantly softer<br>stools (no BSS numbers<br>available)                                      | Significant increase in<br>weekly BM +2.6 (p < 0.01vs<br>baseline and placebo)  | Significant improvements in abdominal discomfort   | [4 |  |
| Kiwifruit powder<br>(freeze-dried)  | Freeze-dried green<br>kiwifruit powder<br>(Zyactinase), 2 capsules<br>x 3/ day;<br>No dose info reported.<br>4-weeks  | Open-label, non-<br>randomised, uncontrolled<br>(Experimental study)<br>Elderly, constipated, n = 41                       | Significantly softer<br>stools (no BSS numbers<br>available)                                      | Significant increase in<br>weekly BM +1.4 (day 21,<br>p < 0.05 vs baseline)   | Significant improvement<br>in feeling of abdominal<br>lightness  | [5 |  |
| Kiwifruit powder<br>(freeze-dried)  | Freeze-dried green<br>kiwifruit with skins<br>(Actiphen / Phenactiv),<br>3,000 mg / day;<br>6-weeks                   | Randomised, double-<br>blind, placebo-controlled,<br>parallel (RCT)<br>Healthy, gastrointestinal<br>symptoms, n = 11       | No significant changes<br>in BSS  | No significant changes<br>in the number of bowel<br>movements   | Significant improvement<br>in gastrointestinal<br>symptoms score   | [6 |  |
| Kiwifruit powder<br>(freeze-dried)  | Freeze-dried green<br>kiwifruit powder (Kivia/<br>Zyactinase), 5.5 g / day;<br>4-weeks                                | Randomised, double-<br>blind, placebo-controlled,<br>parallel (RCT)<br>Healthy, constipated, n = 39                        | Changes in stool form<br>with increases in types<br>3,4 and 5 reported (no<br>averages available) | Significant increase in<br>weekly BM +2.24 (p =0.000<br>vs baseline)  | Significant improvements in bloating and abdominal discomfort  | [7 |  |
| Whole green<br>kiwifruit            | Low-flatulogenic diet plus<br>2 x whole fresh green<br>kiwifruit / day;<br>2-weeks                                    | Near-significant<br>improvement in BSS + 0.5<br>(p = 0.072 vs no kiwifruit)  | Significantly higher BM<br>frequency compared to<br>control group (+2.1 BM/<br>week, p = 0.001)   | Significantly higher BM<br>frequency compared to<br>control group (+2.1 BM/<br>week, p = 0.001)                                     | No significant difference<br>in abdominal symptom<br>scores or abdominal<br>distension                             | [8 |  |
|                                     | 2 x whole fresh green   | Multi-centred,<br>randomised, single-blind,  |   | Significant increase in weekly BM:<br>+1.69 (IBS-C+FC, P < 0.0001)  | Significant improvement  |    |  |
| Whole green<br>kiwifruit            | kiwifruit / day; 4-weeks, 4-week washout Psyllium as positive control   | crossover ( $\overline{R}CT$ )  Functionally constipated, $n = 60$   | Significantly softer stools,<br>BSS +0.6 (FC + IBS-C,<br>p < 0.0001 vs baseline)                  | Significant increase +1.19<br>BM/week in healthy controls<br>(p = 0.0022)   | straining and abdominal  |    |  |
|                                     |   | IBS-C, n = 61<br>Healthy, n = 63   |   | +0.9/week for psyllium (IBS-<br>C+FC groups, p = 0.0007)  | pain   |    |  |
| Whole green<br>kiwifruit            | 2 x whole fresh green<br>kiwifruit / day;<br>4-weeks  | Parallel, partially<br>randomized, exploratory<br>trial  | Significantly softer stools,<br>BSS +0.4 (p = 0.01 vs<br>baseline)                                | Significant increase in weekly BM:<br>+1.0 (p < 0.01 vs baseline)   | Significant improvement in straining (p < 0.01) and bloating (p = 0.02)  | [1 |  |
|                                     | Compared to psyllium and prunes   | Functionally constipated<br>and IBS-C, n = 79  | Prunes but not psyllium significantly improved BSS  | Prunes (+2.7) and psyllium<br>(+1.7) significantly increased<br>weekly BM   | Prunes and psyllium<br>improved straining, but<br>not bloating   |    |  |
| Whole green<br>kiwifruit            | 1 x whole fresh green<br>kiwifruit per 30 kg body<br>weight (2-3 fruit) / day;<br>6-weeks, no washout                 | Randomised,<br>uncontrolled, crossover<br>(preliminary study)<br>Healthy elderly, n = 48                                   | Significant improvement<br>(14%) in consistency<br>(p < 0.0001; NB: not BSS)                      | Near-significant increase in<br>weekly BM +0.54<br>(p = 0.06 vs no kiwifruit)   | Significant improvement<br>in ease (p < 0.0001 vs no<br>kiwifruit)   | [1 |  |
| Whole green<br>kiwifruit            | 1 x whole fresh green<br>kiwifruit per 30 kg body<br>weight (2-3 fruit) / day;<br>3-weeks, no washout                 | Randomised,<br>uncontrolled, crossover<br>(Experimental study)<br>Healthy elderly, n= 38                                   | Significant improvement<br>(12%) in consistency<br>(p < 0.0001; NB: not BSS)                      | Significant increase in<br>weekly BM +0.91<br>(p = 0.012 vs no kiwifruit)   | Significant improvement<br>in ease (p < 0.0001 vs no<br>kiwifruit)   | [1 |  |
| Whole green<br>kiwifruit            | 2 x whole fresh green<br>kiwifruit twice daily;<br>3 days, 2-week washout   | Randomised, crossover  Healthy, n = 14   | Significantly softer stools,<br>BSS +0.6 (p = 0.011 vs<br>control)                                | Significantly higher BM<br>frequency, +0.32 BM/day vs<br>control (p = 0.034)  | No significant difference<br>in adverse symptom<br>scores  | [1 |  |

## **REFERENCES**

- [1] Ansell, J., Butts, C. A., Paturi, G., Eady, S. L., Wallace, A. J., Hedderley, D., & Gearry, R. B. (2015). Kiwifruit-derived supplements increase stool frequency in healthy adults: a randomized, double-blind, placebo-controlled study. Nutrition Research, 401-408.
- [2] KGK Science Inc., 2020, unpublished.
- [3] Kindleysides, S., Kuhn-Sherlock, B., Yip, W., & Poppitt, S. D. (2015). Encapsulated green kiwifruit extract: a randomised controlled trial investigating alleviation of constipation in otherwise healthy adults. Asia Pacific Journal of Clinical Nutrition, 24(3): 421-429.
- [4] Weir, I., Shu, Q., Wei, N., Wei, C., & Zhu, Y. (2018). Efficacy of actinidin-containing kiwifruit extract Zyactinase on constipation: a randomised double-blind place-bo-controlled clinical trial. Asia Pacific Journal of Clinical Nutrition, 27(3): 564-571.
- [5] Uebaba, K., Urata, T., Suzuki, N., Arai, T., Strong, J. M., Oono, S., & Hayashi, H. (2009). Mild laxative and QOL-improving effects of kiwi fruit extract in the elderly an explanatory study on effectiveness and safety. Japanese Journal of Complementary and Alternative Medicine, 6(2): 97-103.
- [6] McIntosh, C. L., & Pohatu, R. (2021). U.S. Patent Application Patent No. 17/166,515.
- [7] Udani, J. K., & Bloom, D. W. (2013). Effects of Kivia powder on gut health in patients with occasional constipation: a randomized, double-blind, placebo-controlled study. Nutrition Journal, 12: 78.
- [8] Caballero, N., Benslaiman, B., Ansell, J., & Serra, J. (2020). The effect of green kiwifruit on gas transit and tolerance in healthy humans. Neurogastroenterology & Motility, 00: e13874.
- [9] Barbara, G., Fukudo, S., Drummond, L., Kuhn-Sherlock, B., Ansell, J., & Gearry, R. (2018). Tu1644-green kiwifruit compared to psyllium for the relief of constipation and improving digestive comfort in patients with functional constipation and constipation predominant irritable bowel syndrome—analysis of three international trial centres. Gastroenterology, 154(6): S-979.
- [10] Cremon, C., Ansell, J., Pagano, I., Kuhn-Sherlock, B., Drummond, L., Barbaro, M. R., . . . Barbara, G. (2018). Su1659 A randomized, controlled, single-blind, cross-over study assessing the effect of green kiwifruit on digestive functions and microbiota in constipated patients. Gastroenterology, 154 (6): S-565-S-566.
- [11] Gearry, R., Barbara, G., Fukudo, S., Ansell, J., Eady, S. L., Wallace, A., . . . Drummond, L. (2017). Tu1614 The effect of Zespri™ green kiwifruit on constipation and abdominal discomfort: A controlled randomized cross-over intervention study. Gastroenterology, 152 (5, Supplement 1): S917.
- [12] Okawa, Y., Nakaya, K., Muratsubaki, T., Okamoto, T., Fuda, M., Endo, Y., . . . Fukudo, S. (2018). Tu1639—Kiwifruit can reduce whole gut transit and symptoms in patients with functional constipation and patients with irritable bowel syndrome with constipation. Gastroenterology, 154 (6): S-977.
- [13] Chey, S. W., Chey, W. D., Jackson, K., & Eswaran, S. (2021). Exploratory comparative effectiveness trial of green kiwifruit, psyllium, or prunes in US patients with chronic constipation. American Journal of Gastroenterology, 00: 1-9.
- [14] Rush, E. C., Patel, M., Plank, L. D., & Ferguson, L. R. (2002). Kiwifruit promotes laxation in the elderly. Asia Pacific Journal of Clinical Nutrition, 11(2): 164-168.
- [15] Wilkinson-Smith, V., Delischaft, N., Ansell, J., Hoad, C., Marciani, L., Gowland, P., & Spiller, R. (2019). Mechanisms underlying effects of kiwifruit on intestinal function shown by MRI in healthy volunteers. Alimentary Pharmacology and Therapy, 49: 759-768.
- [16] Gearry, R., Fukudo, S., Barbara, G., Kuhn-Sherlock, B., Ansell, J., Blatchford, P., ... & Drummond, L. (2022). Consumption of two green kiwifruit daily improves constipation and abdominal comfort—results of an international multicentre randomised controlled trial. Official journal of the American College of Gastroenterology ACG, 10-14309.





