

## Original paper

*Vulvovaginal Candidiasis (VVC) affects 75 per cent of sexually active women at least once in their lifetime<sup>7, 10</sup>. It is reported that five per cent of females who have suffered an acute infection of VVC will experience a recurrence<sup>7</sup>. The mainstay of conventional treatment for VVC is antifungal medication<sup>7</sup>. However, this appears to be unsuccessful in preventing recurring infections<sup>11, 12</sup>.*

# Probiotics in the treatment of vulvovaginal candidiasis

*Imbalances of vaginal micro-flora may give rise to vulvovaginal candidiasis (VVC). This critical review by John Roche and Brian Isbell assesses if probiotics are effective in treating VVC.*

THE VAGINA is a complex microbiological ecosystem. More than 50 different species of bacteria have been recovered from the vaginal tract<sup>1</sup>. These species do not exist independently but continually interact with one another<sup>2</sup>. The Lactobacilli species are reported to be the dominant micro-flora in the vagina<sup>3</sup>. The balance of the vaginal micro-flora is thought to play a key role in the maintenance of vaginal health including an ability to exclude non-indigenous bacteria and maintain homeostasis<sup>2</sup>. The mechanisms behind this are thought to include physical exclusion of pathogenic bacteria, competition for micronutrients, modulation of the vaginal pH and the production of bacteriostatic and bactericidal compounds such

as hydrogen peroxide<sup>1, 2, 4, 5, 6</sup>.

A number of factors are thought to disturb the balance of vaginal micro-flora, including repeated antibiotic use, hormonal imbalances, chronic stress and a processed diet<sup>7, 9</sup>. Opportunistic pathogens, such as the yeast *Candida*, may take advantage of this change in the vaginal environment. Although *Candida* is commonly found in the intestine and vagina of healthy individuals without symptoms<sup>8</sup>, the *Candida albicans* strain is responsible for about 90 per cent of vaginal yeast infections. Vulvovaginal Candidiasis (VVC) affects 75 per cent of sexually active women at least once in their lifetime<sup>7, 10</sup>. It is reported that five per cent of females who have suffered an acute infection of VVC will experience a recurrence<sup>7</sup>. The mainstay of conventional treatment for VVC is antifungal medication<sup>7</sup>. However, this appears to be unsuccessful in preventing recurring infections<sup>11, 12</sup>. Current marketing in the industry promotes probiotics as having the potential to rebalance the micro-flora of the vagina<sup>13</sup>. A critical review of the literature was carried out to assess if the use of probiotics was effective in the treatment of VVC.

### The findings

A number of studies have evaluated the effectiveness of yogurt consumption as a preventative for VVC. In 1992 Hilton et al reported on the efficacy of probiotic yogurt at preventing recurring VVC<sup>14</sup>. In this study, yogurt containing *L. acidophilus* reduced the amount of *Candida* present in the vagina and the recurrence rate of VVC. Hilton et al suggested that *Lactobacilli* compete for the same receptor sites as *Candida* on the epithelium. A second trial by Hilton et al used pasteurised yogurt as a control<sup>15</sup>. This study found no difference between the studies, yet demonstrated a significant concept. The consumption of yogurt containing *L. acidophilus* was associated with an increased colonisation of the rectum and vagina with the bacteria. When *L. acidophilus* was present in the rectal culture the probability of its presence in the vagina was 68 per cent<sup>15</sup>, suggesting that *L. acidophilus* is capable of migrating from the mouth to the vagina via the lower bowel<sup>7, 16</sup>.

A third yogurt study investigated whether live yogurt containing *L. acidophilus* and *Bifidobacteria animalis* could prevent antibiotic-associated VVC<sup>17</sup>. This study found no effect on the rates of infection between live yogurt, commercial yogurt and non-yogurt groups. However, those with a previous history of VVC and who were enrolled in the yogurt groups had fewer infections than those in the non-yogurt group. A possible reason for this was that both yogurt interventions had a significantly high amount of the heat stable *Streptococcus thermophilus* that would have survived the heat treatment of commercial yogurt preparation. *Streptococcus* is a traditional yogurt starter that is thought to be beneficial to health<sup>18, 19</sup>.

A study by Pirota et al aimed to test whether oral or vaginal suppositories containing *Lactobacillus rhamnosus*, *L. delbrucekii*, *L. acidophilus* and *Streptococcus thermophilus* could prevent antibiotic-associated VVC<sup>16</sup>. They concluded that both interventions were ineffective. A second study using some of the same strains, such as *Lactobacillus rhamnosus*, had a different outcome<sup>20</sup>. Prior to the trial five women had significant *Candida* cultures. At the end of the trial four of the five participants returned negative *Candida* cultures<sup>20</sup>. The participants

also experienced a reduction in physical symptoms such as itching. Because the study was not blind it is difficult to say if the outcome was biased.

A third study used both suppositories and oral supplementation of *Lactobacilli acidophilus* to treat VVC<sup>11</sup>. The findings suggest that vaginal suppositories were effective in the prevention of VVC. However, it was acknowledged that the results should be cautiously interpreted due to the small size and demographic nature of the sample population<sup>11</sup>.

### Dosage

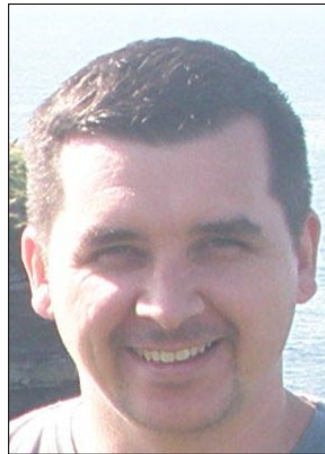
Dosage was an important factor highlighted by these studies. For example, Metts et al found no difference between the rates of VVC infection in the first three months of their study<sup>11</sup>. But in the second three months the infection rates reduced significantly. In the Pirota et al study participants were instructed to use their intervention nightly<sup>16</sup>. Their findings were negative. Hilton et al instructed the suppository to be used twice daily and the results were positive<sup>20</sup>. Witt et al (2009) concluded that *Lactobacilli gasseri* combined with the antifungal medication itraconazole did not add any benefit to the treatment of recurring VVC<sup>21</sup>. However, the probiotic intervention used was extremely low. Participants were instructed to take six probiotic tablets monthly. Therefore, it is possible that if a probiotic is to be considered effective it must be given time to establish itself in the vagina<sup>22</sup>. The literature suggests that 14-28 days should be efficient<sup>22</sup>. Secondly, a daily dosage of at least 800 million live bacteria is considered necessary to have an effect<sup>22</sup>. A higher dosage should allow a sufficient level of bacteria to survive the journey through the gastrointestinal tract<sup>22</sup>. Martinez et al completed a similar study<sup>12</sup>, and found *Lactobacilli. rhamous GR* and *Lactobacilli. reuteri RC* combined with an antifungal medication was effective in reducing VVC rates. A similar study was also conducted by Anukam et al<sup>23</sup>, and their findings suggest that *L. ramous GR-1* and *L. reuteri RC-14* have a role to play in preventing VVC recurrence. It is significant to note that through the use of modern DNA methods Anukam et al (2009) and Martinez et al (2008) supported the findings of earlier studies. Probiotic bacteria can effectively survive the gastric juices and reach the vagina via oral consumption<sup>3</sup>.

### The implications of recent findings

As scientific methods progress our knowledge continues to evolve in relation to understanding of the vaginal ecosystem. It appears it is more unique and diverse than once thought and the generic prescription of probiotics may prove to be unreliable.

An important variable in each study was the strain of bacteria used. *Lactobacillus acidophilus* was used in the majority of studies as it was thought to be the most dominant vaginal micro-flora species<sup>24</sup>. The other strains used were also from the *Lactobacilli* species, including *L. rhammous*, *L. reutueir*, and *L. gasseri*. However, these early studies may have produced unreliable findings due to misdiagnosis of the species. Advances in technology has led to *L. acidophilus* being divided in to sub species, including *L. crispatus* and *L. jensenii*<sup>2,24</sup>.

Therefore, previous identification of *L. acidophilus* as the dominant strain in the vagina may have been incorrect. Earlier studies may have identified a number of strains and presumed it was *L. acidophilus*. Therefore, a reduction in the rates of VVC



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infection may not have been due to *L. acidophilus* but to some other Lactobacilli strain. For example, a study by Antonio et al of 302 women found that *L. crispatus* and *L. jensenii* were the dominant vaginal strains<sup>24</sup>. *L. acidophilus* was not discovered from any of the 302 women in the study. Reid et al reported that in the last six years advances have been made that allowed scientists to decipher the vaginal micro-flora make up<sup>22</sup>. As a result new species have been discovered, including *Lactobacilli iners* which is possibly one of the most common vaginal micro-flora<sup>22</sup>. Kim et al also demonstrated that the vaginal ecosystem is more diverse than once thought<sup>25</sup>. Although 60-70 per cent of their participants demonstrated *Lactobacilli* dominance the rest of the group demonstrated dominance with a variety of other strains, such as *Gardnerella*, *Atopobium*, *Prevotella*, *Pseudomonas* and *Streptococcus*<sup>25</sup>. This significant micro-flora diversity observed among these individuals suggests that defining a healthy vaginal micro-flora is more complex than originally thought<sup>22,25</sup>. This concept aligns itself with the principle of Naturopathy that each person is biochemically unique. It seems individual uniqueness may also be applied to the micro-flora that resides within the body.

This research also appeared to confirm that orally consumed *Lactobacilli* have the ability to reach the vagina via the bowel. This concept is important for two reasons. Firstly orally consumed bacteria can travel from the rectum to the vagina. Secondly the rectum could be the source of a recurring VVC infection due to an overgrowth of *Candida* in the lower bowel<sup>13,7</sup>. This could explain why antifungal medication fails to resolve recurring VVC<sup>7,14</sup>. Therefore, if the large intestine acts as a reservoir for *Candida* then it is essential to rebalance the micro-flora of both the vagina and the lower bowel in a treatment protocol of VVC.

### Implications for Naturopathic Practice

Naturopathic approaches to dietary therapy that may provide relief include:

1. Reduce/remove processed foods such as refined carbohydrates as they may contribute to dysbiosis in the lower bowel<sup>9</sup>.
2. Increase intake of whole-grains, fruits and vegetables as dietary fibre is a major food source of the dominant bacteria of the lower intestine bifidobacteria. Bifidobacteria are thought to suppress and compete with *Candida* in the lower bowel<sup>9,5</sup>.

This research shows that a broad-spectrum probiotic either in

supplement or yogurt form combined with a natural antifungal and local suppository applications could prove to be more effective than single strained supplements.

Single strained *Lactobacilli* supplements may fail to suppress the source of a recurring VVC infection in the large intestine. Secondly, due to the uniqueness of each individual's microflora a single-strained supplement such as *L. acidophilus* may simply be ineffective. Lastly, the intervention used should contain significant quantities of bacteria and be consumed for an appropriate length of time.

#### References:

- Cribby, S., Taylor, M. and Reid, G., (2008). Vaginal Microbiota and the Use of Probiotics. *Sexually transmitted infections*, 36, 37.
- Yamoto, T., Zhou, X., Williams, C.J., Hochwalt, A. and Forney, L.J., (2009). Bacterial populations in the vaginas of healthy adolescent women. *Journal of pediatric and adolescent gynecology*, 22(1), 11-18.
- Morelli, L., Zonenenschain, D., Del Piano, M. and Cognein, P., (2004). Utilization of the intestinal tract as a delivery system for urogenital probiotics. *Journal of clinical gastroenterology*, 38, S107.
- Song, Y.L., Kato, N., Matsumiya, Y., Liu, C.X., Kato, H. and Watanabe, K., (1999). Identification of and hydrogen peroxide production by fecal and vaginal lactobacilli isolated from Japanese women and newborn infants. *Journal of clinical microbiology*, 37(9), 3062.
- Rastall, R.A., Gibson, G.R., Gill, H.S., Guaner, F., Klaenhammer, T.R., Pot, B., Reid, G., Rowland, I.R. and Samders, M.E., (2006). Modulation of the microbial ecology of the human colon by probiotics, prebiotics and synbiotics to enhance human health: An overview of enabling science and potential applications. *FEMS microbiology ecology*, 52(2), 145-152.
- Boris, S., Suarez, J.E., Vazquez, F. and Barbes, C., (1998). Adherence of human vaginal lactobacilli to vaginal epithelial cells and interaction with uropathogens. *Infection and immunity*, 66(5), 1985.
- Sobel, J.D., (2007). Vulvovaginal candidosis. *The Lancet*, 369 (9577), 1961-1971.
- Lopez-Martinez, R., 2010. Candidosis, a new challenge. *Clinics in dermatology*, 28(2), 178-184.
- Hawrelak, J.A. and Myers, S.P., (2004). The causes of intestinal dysbiosis: a review. *The alternative Review*, 9 (2) 44.
- Chapple, A., Hassell, K., Nicolson, M. and Cantrill, J., (2000). You don't really feel you can function normally: women's perceptions and personal management of vaginal thrush. *Journal of Reproductive and Infant Psychology*, 18(4), 309-319.
- Metts, J., Famula, T., Tenev, N., Clemens, R. (2003). *Lactobacillus acidophilus*, Strain NAS (H202 positive), in reduction of recurrent candidal vulvovaginitis. *The Journal of Applied Research*. 3(4), 341.
- Martinez, R., Franceschini, S., Patta, M., Quintana, S., Candido, R., Ferreria, J., DE Martinis, E. and Reid, G., (2009). Improved treatment of vulvovaginal candidiasis with fluconazole plus probiotic *Lactobacillus rhamnosus* GR-1 and *Lactobacillus reuteri* RC-14. *Letters in applied microbiology*, 48(3), 269-274.
- Gibson, G., (2005). The rise and rise of probiotics. *Biologist*, 52(2), 95-98.
- Hilton I, E., Isenberg, H.D., Alperstein, P., France, K. and Borenstein, M.T., (1992). Ingestion of yogurt containing *Lactobacillus acidophilus* as prophylaxis for candidal vaginitis. *Annals of Internal Medicine*, 116(5), 353.
- Shalev, E., Battino, S., Weiner, E., Colodner, R. and Keness, Y., (1996). Ingestion of yogurt containing *Lactobacillus acidophilus* compared with pasteurized yogurt as prophylaxis for recurrent candidal vaginitis and bacterial vaginosis. *Archives of Family Medicine*, 5(10), 593.
- Pirotta, M., Gunn, J., Chondros, P., Grover, S., O'Malley, P., Hurley, S. and Garland, S., (2004). Effect of lactobacillus in preventing post-antibiotic vulvovaginal candidiasis: a randomised controlled trial. *British medical journal*, 329(7465), 548.
- Conway, S., Hart, A., Clark, A. and Harvey, I., (2007). Does eating yogurt prevent antibiotic-associated diarrhoea?: A placebo-controlled randomised controlled trial in general practice. *The British Journal of General Practice*, 57(545), 953.
- Jin, L., Tao, L., Pavlova, S., SO, J., Kiwanuka, N., Namukwaya, Z., Saberbbein, B. and Wawer, M., (2006). Species diversity and relative abundance of vaginal lactic acid bacteria from women in Uganda and Korea. *Journal of applied microbiology*, 102(4), 1107-1115.
- Guarner, F., Perdigon, G., Cortheir, G., Salminen, S., Koletzko, B. and Morelli, L., (2007). Should yogurt cultures be considered probiotic? *British Journal of Nutrition*, 93(06), 783-786.
- Hilton, E., Rindos, P. and Isenberg, H., 1995. *Lactobacillus* GG vaginal suppositories and vaginitis. *Journal of clinical microbiology*, 33(5), 1433.
- Witt, A., Kaufmann, U., Bitschnau, M., Tempfer, C., Özbal, A., Hayouglut, E., Gregor, H. and Kiss, H., (2010). Monthly Itraconazole Versus Classic Homeopathy for the Treatment of Recurrent Vulvovaginal Candidiasis: A Randomized Trial. *Obstetrical & gynecological survey*, 65(1), 26.
- Reid, G., Dols, J. and Miller, W., (2009). Targeting the vaginal microbiota with probiotics as a means to counteract infections. *Current Opinion in Clinical Nutrition & Metabolic Care*, 12(6), 583.
- Anukam, K.C., Duru, M.U., Eze, C.C. and Reid, G., (2009). Oral use of probiotics as an adjunctive therapy to fluconazole in the treatment of yeast vaginitis: A study of Nigerian women in an outdoor clinic. *Microbial Ecology in Health and Disease*, 21(2), 72-77.
- Antonio, M.A.D., Hawes, S.E. and Hiller, S.L., (1999). The identification of vaginal *Lactobacillus* species and the demographic and microbiologic characteristics of women colonized by these species. *The Journal of infectious diseases*, 180, 1950-1956.
- Kim, T.K., Thomas, S.M., HO, M., Sharmia, S., Reich, C.I., Frank, J.A., Yeater, K.M., Biggs, D.R., Nakamura, N. and Stumpf, R., (2009). Heterogeneity of vaginal microbial communities within individuals. *Journal of clinical microbiology*, 47(4), 1181.

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