

FIXATION ON HISTOLOGY

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Diet, DIY & prevention of cervical cancer

Cervical cancer is one of the most preventable and treatable types of cancer. In 2020, it was estimated that 600,000 women worldwide were diagnosed with the disease and more than 340,000 dying as a result. With cervical cancer often linked to lifestyle factors, a well-balanced diet can help reduce risk by preventing infection and transformation of cervical cells. Pathogens such as the human papillomavirus (HPV) are known to induce oxidative stress and the damage to the cellular DNA that results from infection often progresses to cancer. Food containing elevated quantities of antioxidants such as folate and flavonoids are known to provide health benefits and studies have shown that dietary supplements of antioxidants reduce the risk of cervical cancer in women who are infected with HPV (1). Equally, seaweeds have also been observed to promote health and wellbeing (2). For example, the edible algae *Porphyra umbilicalis*, commonly found between the west coast of mainland Britain and Ireland, is used to prepare laverbread, a Celtic delicacy that is popular in Wales (Figure 1). Rich in protein, iodine and vitamins, this seaweed has chemo preventative properties that blocks further development of pre-cancerous lesions induced by HPV (3). Additionally, *Chondrus crispus*, a red algae more commonly known as Irish or carrageen moss, has been used for centuries in traditional cooking (Figure 1). Grown abundantly along rocky parts of the North Atlantic coasts, this algae is widely used as a gelling agent in everyday products such as baby food, ice cream and toothpaste. Crucially, this seaweed has also shown to inhibit pathogens such as HPV from infecting and transforming human cells (4). This creates the question as to why these algae are able to prevent HPV from promoting carcinogenesis.

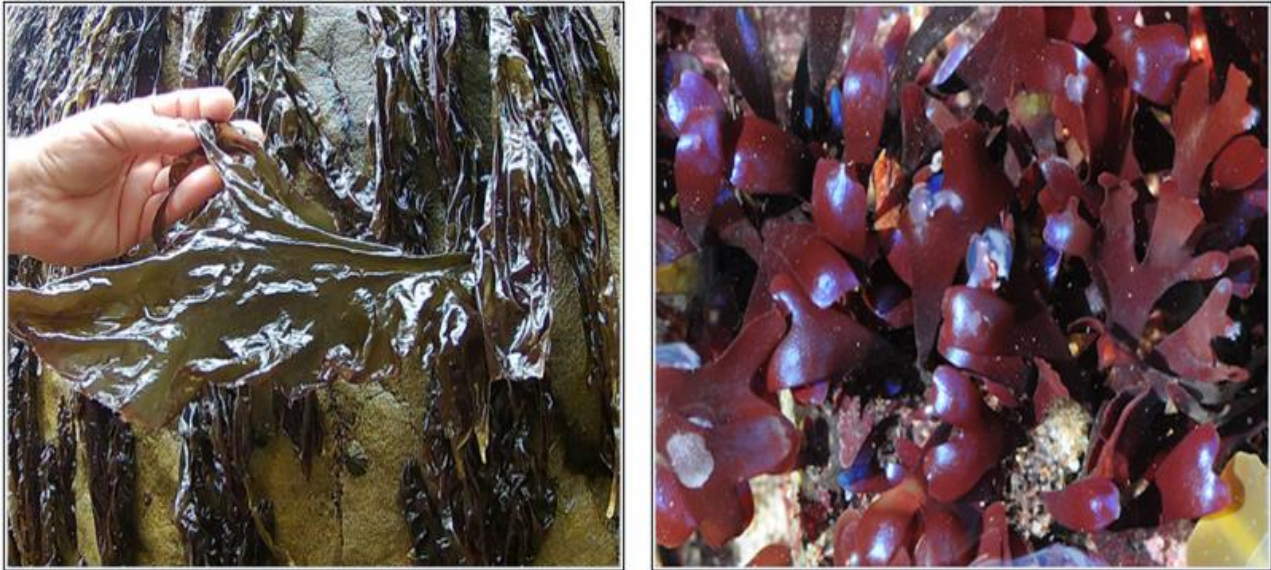


Figure 1. The seaweeds *Porphyra umbilicalis* (left) and *Chondrus crispus* (right)

The answer lies in the component known as carrageenan, a sulphated polysaccharide that is common to both seaweeds (2). By adhering to surface viral proteins, carrageenan interferes with the ability of viruses such as HPV to attach to and invade human cells. More significantly, the HPVs associated with genital disease are a thousand times more susceptible to carrageenan than other infective organisms such as herpes simplex and the human immunodeficiency virus (4). The fact that some infant formulas contain carrageenan raises the possibility that baby feeds could prevent juvenile laryngeal papillomatosis in the new born since the disease is initiated by vertical transmission of HPV during birth from mothers who have genital warts. Carrageenan is also a constituent of microbicides (lubricant gels) and clinical trials have shown that regular use of these products during sexual activity is highly effective at preventing the spread of HPV that are associated with genital cancers (5). With the potency of antioxidants and carrageenan already established in preventing HPV-related diseases, it is evident they have a significant role to play in the global fight against cervical cancer. Nevertheless, there are other, perhaps more important, precautionary measures to consider such as cervical cytology screening, molecular testing for HPV and vaccination. Existing programmes are typically reliant on attendance at health centres where smears are taken by clinicians prior to dispatch to central laboratories for staining and screening (Figure 2).

In developing countries, the burden from this disease is greater because of the complexities associated with implementing screening and testing programmes. In order to overcome these

difficulties, an effective approach recommended by the World Health Organisation is the use of vaginal self-sampling for the early detection of cervical cancer (6). This method has proved acceptable in terms of use as no pelvic examination is necessary. Participation in vaginal self-sampling offers convenience and benefits to those women who face barriers in attending cytology screening programmes as a result of logistical or personal concerns such as emotional and physical trauma.

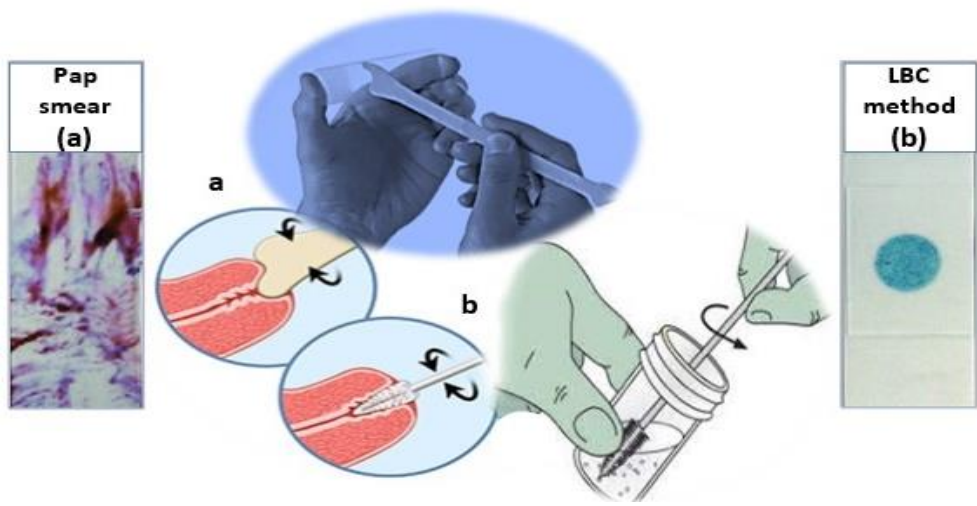


Figure 2. Cervical smear preparation using (a) the conventional Papanicolaou method and (b) liquid-based cytology (LBC)

Self-sampling offers opportunities to those individuals who have never been screened as well as to those who may have been under screened. Devices such as sanitary products, swabs and brushes are readily available for self-sampling at home or clinic settings (Figure 3). With the vaginal drift of exfoliated cervical cells related to the menstrual cycle, the convenience of sanitary products is a viable option for the testing of high-risk HPV, regardless of the duration that the cervicovaginal cells have been exposed to them.

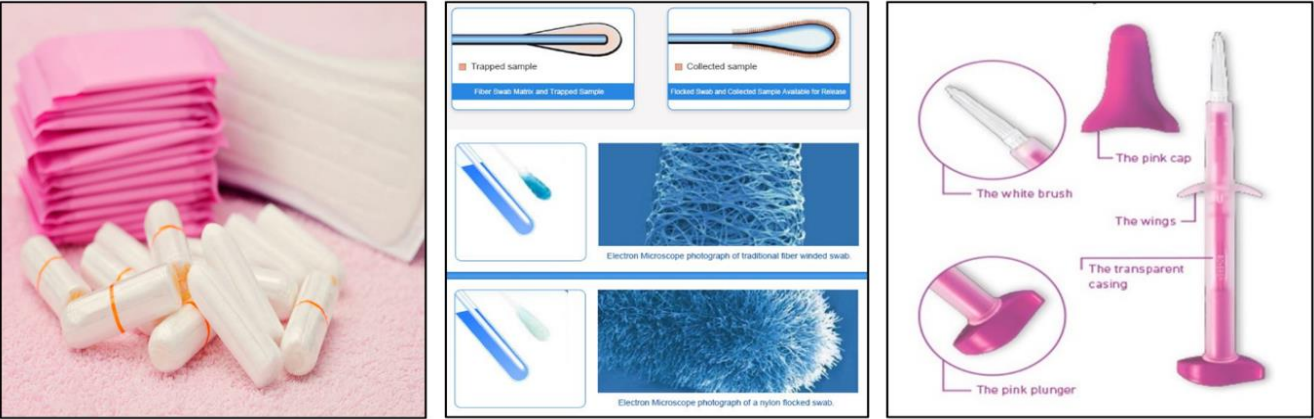


Figure 3. Vaginal self-sampling devices: Sanitary products (left), swabs (centre) & brushes (right)

The late proliferative and early secretory phases which span ovulation during the menstrual cycle provides the greatest volume of exfoliated cells suitable for testing (7). When these samples are assessed for high-risk HPV, menstrual blood flow, vaginal self-collected and clinician-collected samples all show good concordance when the processes are compared (8,9).

With the global uptake of conventional cervical screening poor due to geographic, socioeconomic and cultural barriers, vaginal self-sampling is a valuable option for providing those populations with access to screening programmes. With the further potential of urine sampling as a low cost, non-invasive tool for analysing high-risk HPV, the possibilities are endless for preventing cervical cancer worldwide (11). However, encouraging and educating women to conduct self-sampling whilst giving assurances to those who may distrust results will certainly be challenging. In addition, missed opportunities to converse with clinicians about other concerns and the management of follow-up of HPV positive patients are further barriers.

Further reading

1. Dietary antioxidant intake and human papillomavirus infection: Evidence from a cross-sectional study in Italy (Barchitta et al, 2020). *Nutrients* 2020;12:1384. <https://www.mdpi.com/2072-6643/12/5/1384>
2. Anti-cancer activity of porphyran and carrageenan from red seaweeds (Liu et al, 2019). *Molecules* 2019;24:4286. <https://www.mdpi.com/1420-3049/24/23/4286>
3. Dietary supplementation with the red seaweed *Porphyra umbilicalis* protects against DNA damage and pre-malignant dysplastic skin lesions in HPV-transgenic mice (Santos et al, 2019). *Marine Drugs* 2019;17:0615. <https://www.mdpi.com/1660-3397/17/11/615>
4. Antiviral activities of algal-based sulfated polysaccharides (Panggabean et al, 2022). *Molecules* 2022;27:1178. <https://doi.org/10.3390/molecules27041178>
5. Are bioactive molecules from seaweeds a novel and challenging option for the prevention of HPV infection and cervical cancer therapy? - A review (Moga et al, 2021). *International Journal of Molecular Sciences* 2021;22:629. <https://doi.org/10.3390/ijms22020629>
6. Results of a phase 1, randomized, placebo controlled first-in-human trial of griffithsin formulated in a carrageenan vaginal gel (Teleshova et al, 2022). *PLoS ONE* 2022;17(1): e0261775. <https://doi.org/10.1371/journal.pone.0261775>

7. Worldwide use of HPV self-sampling for cervical cancer screening (Serrano et al, 2022). Preventive Medicine 2022;154:106900. <https://doi.org/10.1016/j.ypmed.2021.106900>
8. Effects of menstrual cycle on the accumulation of HPV-infected cells exfoliated from the cervix that drift into the vagina (Okodo et al, 2022). Microorganisms 2022;10:693. <https://www.mdpi.com/2076-2607/10/4/693>
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11. Urine HPV in the context of genital and cervical cancer screening - An update of current literature (Daponte et al, 2021). Cancers 2021;13:1640. <https://www.mdpi.com/2072-6694/13/7/1640>

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