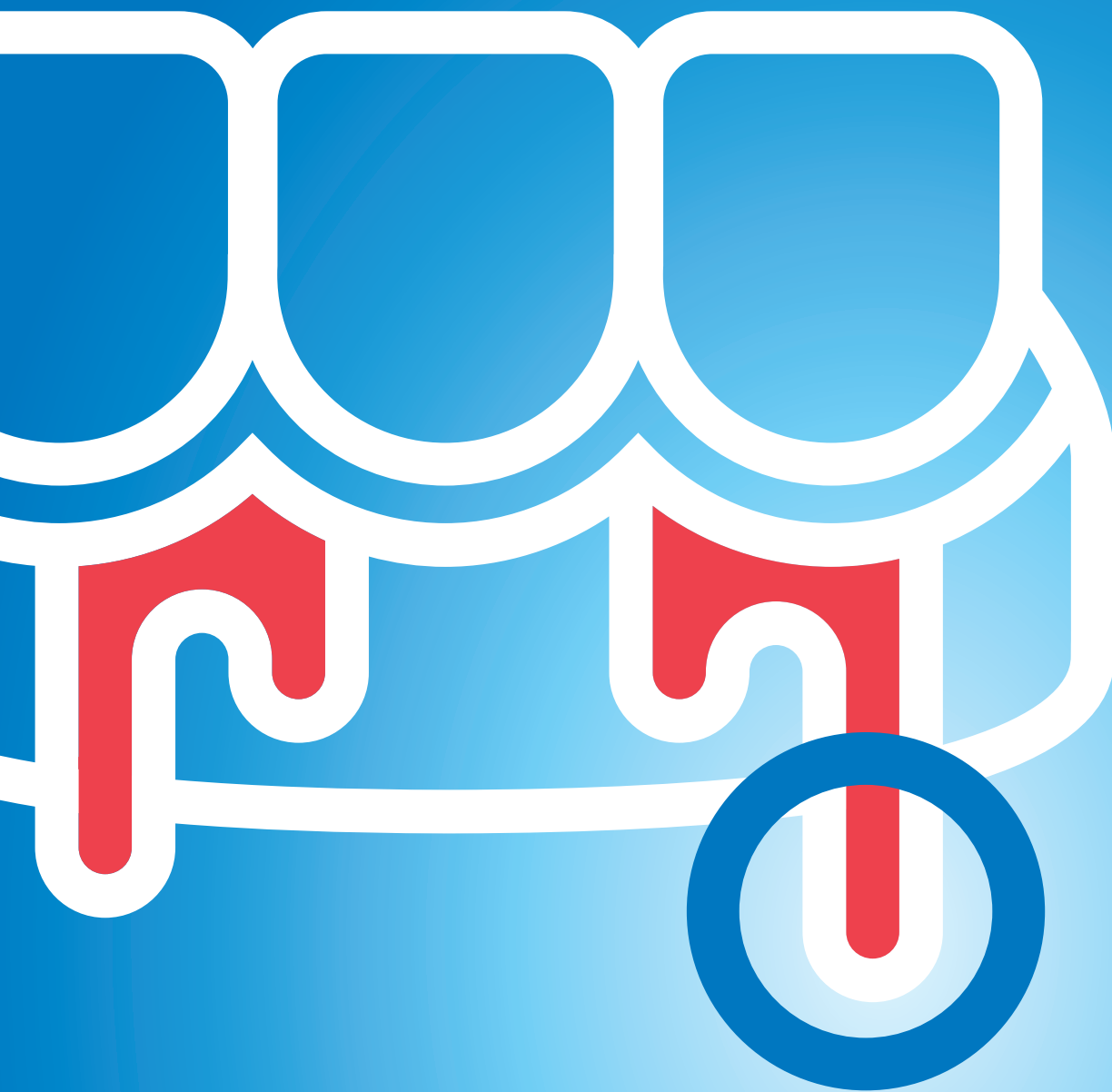


ORAL HEALTH &
GINGIVITIS

FACT FILE

GENGIGEL[®]
Hyaluronic Acid



HOW CAN ORAL DISEASE AFFECT HUMAN HEALTH?

Oral health is the condition of the mouth, teeth, and orofacial structures that enables people to perform essential functions such as eating, breathing and speaking, and to engage in social activities without pain, discomfort or embarrassment. Oral health can be weakened by a wide range of diseases that affect 3.5 billion people worldwide and span the life course from childhood to old age. The most common diseases that affect oral health include dental caries, periodontal (gum) disease, tooth loss, and oral cancer (Bessa et al., 2022). **More than 40% of adults report having experienced oral pain in the past year** (CDC, Center for Disease Control and Prevention), and **periodontal disease affects between 20% and 50% of the world's population** (Karakostas

et al., 2022). Periodontal disease is primarily the result of infection and inflammation of the gums and bone that surround and support the teeth. Most periodontal diseases can be broadly divided into gingivitis and periodontitis (PD) depending on the type/degree of damage (Page and Kornmann, 2000). **Gingivitis is a common inflammation of the soft tissues around the neck of the tooth associated with a shift in the local microflora** (Klukowska et al., 2015) but if left untreated, damage to the supporting tissues can progress to PD (Schätzle et al., 2003). In this case, an irreversible inflammation

periodontal disease affects 20% ÷ 50% of the world's population

> 40% adults report having experienced oral pain

of the periodontium leads to tissue destruction and bone resorption, often resulting in loss of the supporting structure and teeth (Costa et al., 2023). Although oral diseases are often considered separately from other chronic

conditions, evidence suggests that PD is associated with chronic diseases such as diabetes, obesity, weakened immune system and cardiovascular disease (Kumar et al., 2019). Tobacco use is also an important risk factor for gum disease. Recently, a systematic review found an association between PD and adverse pregnancy outcomes (Saadaoui et al., 2021). Although evidence is limited, it has been proposed that oral health may also affect female fertility through a biological mechanism related to inflammation (Ricci et al., 2022).

HOW DOES GINGIVITIS AFFECT ORAL HEALTH?

Gingivitis is an inflammatory disease of the gum tissue, most commonly caused by a bacterial infection in or near the gingival sulcus (Bessa et al., 2022). It is the most common periodontal disease and **can affect anyone, at any age**. There are several forms of gingivitis, that differ in clinical presentation, duration of infection, severity and etiology. Depending on the etiology, gingivitis can be classified into different types: plaque-induced gingivitis; nutritional gingivitis due to vitamin C deficiency; hormonal gingivitis during pregnancy; drug-induced gingivitis as a side effect (Marchesan et al., 2000). However, the chronic form of gingivitis caused by plaque formation is considered the most common variant (Trombelli et al., 2018). Depending on the severity and progression of symptoms which usually manifest as red, swollen or infected gums, gingivitis can be classified as mild, moderate or severe. The accumulation of microorganisms around the teeth leads to the release of proinflammatory cytokines, such as IL-1 and TNF- α , recruitment of inflammatory cells, and periodontal inflammation. These cy-

tokines also upregulate matrix metalloproteases, which can then degrade collagen and cause loss of periodontal attachment and destruction of bone (Maderal et al., 2021). This process is complex and multifactorial. Several factors, such as dysbiosis, genetic, environmental, and behavioral risk factors lead to inter- and intra-individual differences in the onset of periodontal disease, the pattern of progression, and the response to therapy (Kumar et al., 2019). This is true even when "normal" oral hygiene is practiced. Although maintaining good oral hygiene is the first-line of treatment for gingivitis, it is still not fully understood why its effectiveness varies from person to person. Moreover, no universal pattern has been found across hosts (Hajishengallis and Lamont, 2021). Recently, the concept of dysbiosis triggered by various environmental changes and critical pathogens has gained support (Hajishengallis, 2015). However, such altered dysbiotic microbiota can form stable communities that can be suppressed, but not eliminated, by antimicrobial therapies (Ide et al., 2022).

WHY RESORT TO NON-DRUG TREATMENTS?

The main goal in the treatment of gingivitis is to reduce inflammation. Initial treatment of oral disease includes control of risk factors, oral hygiene, and supra- and subgingival debridement of teeth by professional mechanical plaque removal. Antiseptic agents administered via toothpastes or mouthwashes can support mechanical oral hygiene. However, there is evidence that conventional formulations containing certain detergents may exacerbate some ulcerative conditions in the oral cavity (Tadin et al., 2019). Chemical methods of plaque removal are widely accepted as clinically effective in the treatment of periodontal disease. However, they are often not well tolerated by patients due to discomfort and pain that may be caused by various ingredients such as flavorings, astringents, essential oils and preservatives (Tadin



et al., 2019). Host modulation therapy with anti-inflammatory drugs, such as nonsteroidal anti-inflammatory drugs, has also been shown to reduce gingivitis but is not recommended in clinical practice because of known side effects. Therefore, treating mucosal inflammation and eliminating lesions can lead to patient compliance issues and the risk of drug interactions (ide et al., 2022). The use of coating devices containing hyaluronic acid (HA) has been proposed to promote healing by acting as a barrier that improves water retention and facilitates collagen and elastin formation, and protects the lesion from the surrounding oral environment, with a safe anti-inflammatory effect (Sridharan and Sivaramakrishnan, 2021; Chen and Abatangelo, 1999).

WHY HIGH MOLECULAR WEIGHT HYALURONIC ACID?

Hyaluronic acid (HA) is a non-sulfated glycosaminoglycan (GAG) widely distributed in neural, epithelial and connective tissues, including the periodontium. As one of the major components of the extracellular matrix (ECM), HA contributes significantly to tissue regeneration, inflammatory response, and angiogenesis, and plays a key role in wound healing (Graça et al., 2020). The properties of HA are directly related to its molecular weight. High molecular weight hyaluronic acid (HMW-HA) inhibits cell differentiation and promotes cell proliferation, is involved in tissue regeneration, wound healing, epithelial integrity, embryogenesis, plasma protein distribution, matrix structuring and water



homeostasis (Valachová et al., 2021). HMW-HA has a remarkable hydration capacity and can swell to many times its original volume upon water uptake, improving tissue hydration and cell resistance to mechanical damage. This biopolymer is commonly used in the treatment of gingivitis, recession, and periodontal pockets due to its properties, and as a component of grafts and implants (Iviglia et al., 2019). In addition, HA can act as a stable barrier against viral and bacterial invasion, promoting regeneration in oral cavity diseases (Iviglia et al., 2019).

Why Gengigel®?

Hyaluronic acid deficiency resulting from oral tissue injury leads to free water imbalance and delayed healing. **Gengigel®**, with its **HMW-HA-based composition**, **protects the gingival mucosa by promoting the natural healing and recovery process of the tissue**. Thanks to its bioadhesive and film-forming properties, it forms a stable barrier that preserves the microenvironment of the mucosal surface and accelerates mucosal healing by maintaining the action of HMW-HA over a long period of time while delaying the absorption and excretion of HMW-HA. The ability of HMW-HA to retain large amounts of water helps **Gengigel®** maintain extracellular fluid balance and promote the edema resorption in inflammatory conditions, providing rapid relief to inflamed oral tissues. Importantly, hyaluronic acid has no local or systemic pharmacological effects on the mucosa. A recent systematic review of 38 randomized clinical trials reported that the concomitant use of HA in gingivitis (8), nonsurgical (20) and surgical (10) periodontal therapy improved patients' clinical parameters, including periodontal probing depth, periodontal inflam-

mation, and clinical attachment level (gingival recession) while reducing the prescription of non-steroidal anti-inflammatory drugs (Karakostas et al, 2022). In most studies, HA was used as a gel, in some studies as a mouthwash or spray, and in one study as fibers. In all cases, HA was found to be extremely safe, with no contraindications or side effects reported. **The evidence on Gengigel® includes clinical data from high-quality prospective, comparative studies** (Polepalle et al. 2015; Gupta 2017; Al-Shammari et al. 2018; Ibraheem et al., 2022). **The studies covered various indications for Gengigel®, including the treatment of clinical signs associated with periodontal disease and gingivitis following surgical periodontal therapy or the healing of extraction wounds.** Patients were treated with the gel or spray formulation, either with a single application at the time of surgery, or with multiple applications following periodontal surgery/treatment. **Gengigel® was shown to**

be an effective treatment for restoring healthy gums and controlling the inflammatory process at various stages of periodontal disease, providing a beneficial effect on early postoperative healing following extraction.



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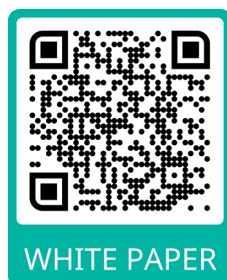
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