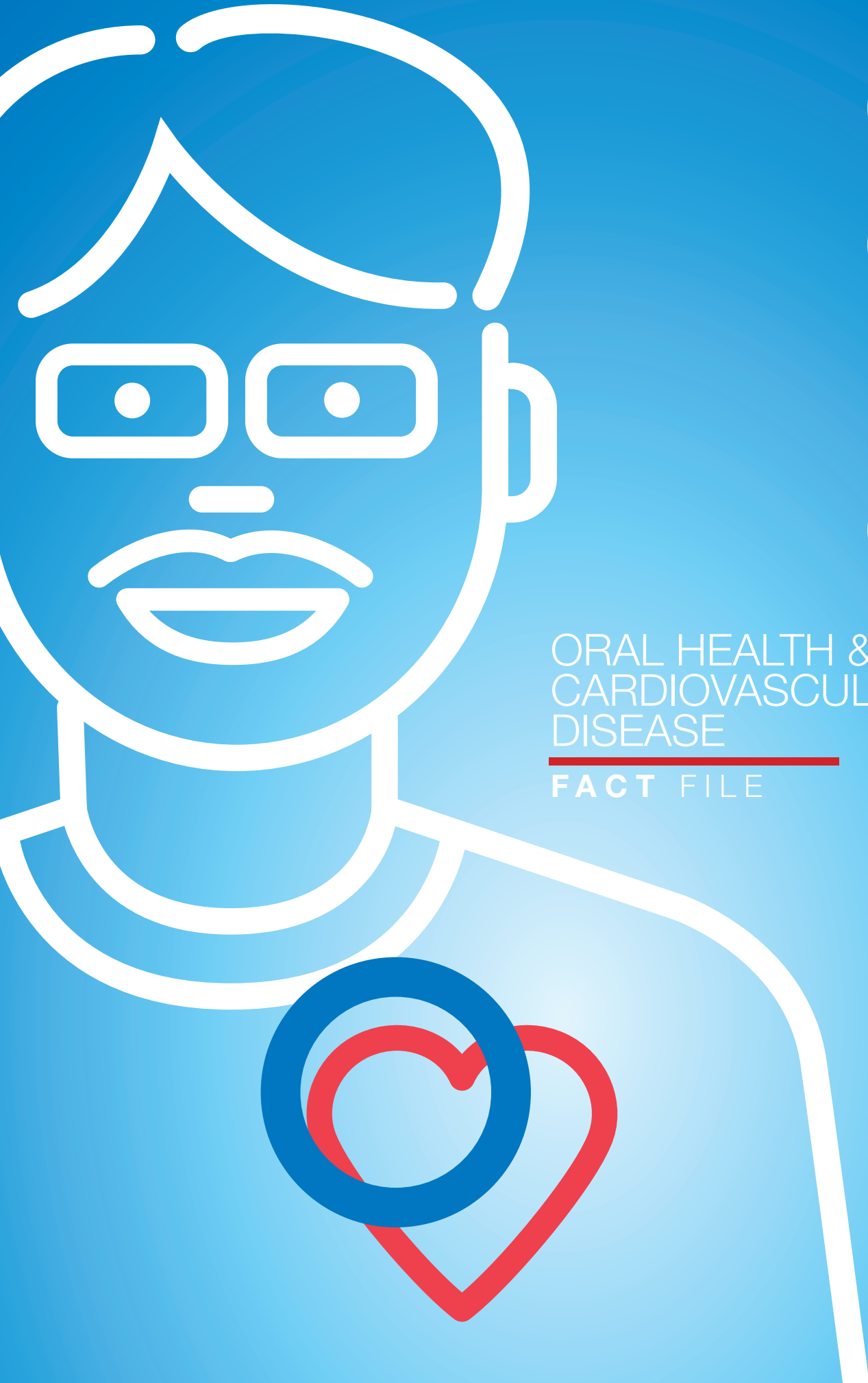


GENGIGEL[®]

Hyaluronic Acid

ORAL HEALTH &
CARDIOVASCULAR
DISEASE

FACT FILE



HOW CAN ORAL HEALTH AFFECT CARDIOVASCULAR SYSTEM HEALTH?

In Europe cardiovascular disease (CVD) is responsible for 3.9 million deaths (45% of deaths), with ischaemic heart disease, stroke, hypertension (leading to heart failure) being the major cause of CVD related deaths. Periodontal diseases (PD), chronic conditions with a high prevalence and severe

3.9mln
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for
cardiovascular
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periodontitis, affecting 11.2% of the world's population, is the sixth most common human disease (Sanz et al. 2019). Periodontal diseases are caused by pathogenic microbiota (pathobionts) in the dental plaque formed on the hard root surface adjacent to the supporting soft tissues (Kassebaum et al. 2017). As more and more data suggest that

chronic inflammatory conditions may increase the risk of cardiovascular disease (Willerson et al. 2004), attention has been drawn to periodontitis and its possible association with CVD.

Indeed, there is increasing evidence in the literature that PD can have negative cardiovascular effects (Naderi et al. 2020).

11.2%
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HOW DOES PERIODONTITIS FAVOUR THE ONSET OF CARDIOVASCULAR DISEASES?

Although a clear association between periodontal and cardiovascular diseases has been well characterized, a causal relationship has not yet been established. A clear association documented in literature is that poor oral hygiene leads to bacteremia, which in turn can cause bacterial growth over atherosclerotic coronary artery plaques and potentially worsen coronary artery disease (Lockhart et al. 2009). PD encapsulates a broad range of chronic inflammatory conditions that affect the gingiva, bone and the periodontal ligaments supporting the architecture of the teeth. The microorganisms involved in PD (mainly gram-negative anaerobic bacteria) can be found in a complex biofilm in the oral cavity known as the dental plaque (Gunaratnam 1992; Moore, 2000). One important factor that facilitates the translocation of bacteria into the blood stream is that the oral

cavity is highly vascularized and the epithelium is relatively thin (Leishman et al. 2010). Therefore, procedures such as brushing and mastication might disturb this epithelium and possibly contribute to an occult or overt bacteremic state (Schenkein et al. 2013). Moreover, as periodontitis is considered an inflammatory condition, dilatation of the periodontal vasculature can facilitate bacteremia. It is known that inflammation is critical to the development of atherosclerosis (Libby et al. 2002) and that treating inflammation is associated with a reduction in cardiovascular risk (Verma et al. 2017). Thus, treating periodontitis to restore a healthy periodontium can help reduce overall inflammation in the body, which in turn plays an important role in the prevention of cardiovascular disease (Pryamvara et al. 2020).

WHY RESORTING TO NON-DRUG TREATMENTS?

Dealing with cardiovascular diseases means that several districts of the organism are involved and that different therapeutic options might be necessary. Periodontal therapy (scaling, root planing, antibiotic treatment) has been shown to reduce levels of pro-inflammatory markers (CRP, TNF- α , and IL-6), further corroborating the periodontium as a source for these inflammatory mediators (Arroll et al. 2010). First-line treatments for periodontal diseases include non-pharmacological interventions such as effective daily oral hygiene with mouthwashes, fluoride-



containing toothpastes and even plaque biofilm and tartar deposits removal through scaling and root planing (Wilder et al. 2016). These activities increase clinical attachment levels, reduce probing depths and bleeding on probing. Nevertheless, the effectiveness of the treatments depends on the successful eradication of bacteria residing in deep pockets. Hence, resorting to non-drug treatments such as creating a barrier to prevent the entrance of pathogens through the oral cavity might be a first line protection also for cardiovascular diseases.

WHY HIGH MOLECULAR WEIGHT HYALURONIC ACID?

HA is a natural and unbranched polymer belonging to a group of heteropolysaccharides called glycosaminoglycans (GAGs) diffused in the epithelial, connective and nervous tissues of vertebrates (Fraser et al. 1997). HA is major component of the ECM, particularly abundant during embryogenesis, in tissues undergoing rapid growth and development, during repair and regeneration, and in association with aggressive malignancies (Erickson et al. 2012). **HA has many different functions, including maintenance of tissue homeostasis and cell surface protection, but it is also involved in many physiological processes, such as cell attachment, migration and proliferation, wound healing, and regulation of immune response and inflammation** (Kavasi et al. 2017). High molecular weight hyaluronic acid (HMWHA) is deposited in normal



tissues and interacts with other components of the ECM to control the ECM structural organization and signaling. In addition, endogenous HMWHA possesses enhanced anti-angiogenic, anti-inflammatory and immunosuppressive properties (Kavasi et al. 2017). The amphophilic nature of HMWHA allows this molecule to trap large amounts of water while binding to hydrophobic molecules such as cell membrane lipids. This property is relevant to the control of hydration and helps to delay the passage of viruses and bacteria through the hyaluronan-rich pericellular zone, as well as during inflammatory processes (Chen and Abatangelo 1999). **Clinical studies have shown that HA accelerates the healing of various types of wounds, including burns, epithelial surgical wounds, and chronic wounds** (Shaharudin and Aziz 2016).

Why Gengigel®?

Gengigel® is a specific and innovative treatment for gingivitis and periodontitis that relies on the action of its main component, high molecular weight hyaluronic acid (HMWHA) to make the product strongly bioadhesive, an effect that may be enhanced by using a calibrated mixture of additional glycopolymers. Because of its adhesive properties, Gengigel® sticks to the oral mucosa long enough to promote the activation of physiological tissue repair processes which improve the healing response and reduce healing time. In addition, the presence of high molecular weight hyaluronic acid helps Gengigel® maintain the balance of extracellular fluids and promotes the resorption of oedema in inflammatory conditions, rapidly reducing the associated pain. Last but



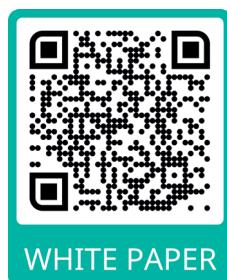
not least, it protects the oral mucosa by preserving the micro-environment of the mucosal surface and by regularizing the growth of bacterial flora. The evidence on Gengigel® includes clinical data from high-quality prospective, comparative studies (Gupta, 2017; Al-Shammari, 2018; Polepalle, 2015). The studies covered different Gengigel®

indications, including treatment of clinical signs associated with periodontal disease or gingival inflammation following surgical periodontal therapy. In all cases, patients were treated with the gel formulation, either in a single application at the time of surgery, or with multiple applications following periodontal surgery/treatment. Gengigel® proved to be an effective treatment in controlling the inflammatory process and gingival bleeding at various stages of periodontal disease.



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RICERFARMA S.R.L.
www.ricerfarma.com

Via Egadi, 7 - 20144 Milano – Italy
info@ricerfarma.com