Particles for Osteoarthritis Treatment: Injected Wet Particulate of Collagen-Elastin-Glycosaminoglycan Matrix into Synovial Fluid, Mechanically Cushion Joint with Long Duration

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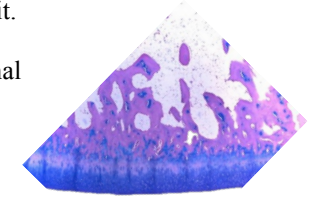
Purpose: MasterGel Hydrophilic Biomaterial (**MHB**) was created and developed by Gel-Del, generating issued patents (8 US, 12 foreign) and products [1,2,5]. MHB studies have demonstrated medical potential for drug delivery, blood vessels, tissue bulking, stent & catheter coatings, and more [1,2]. Here, MHB particles were injected into joints with osteoarthritis (**OA**) to provide safe, slippery micronized cushions that mechanically augment the articulating cartilage, ameliorating pain, and protecting joint from further injury. MHB particles are singulated, >90% hydrated, insoluble, 70-110 microns (larger than synovium pores), and absorb-release synovial fluid from joint articulations. MHB provides joint technology to the medical device industry as a synovial fluid particle scaffold that not only is well tolerated, its extracellular matrix (ECM) component structure can also assist the regenerative healing process to provide a long-lasting and unique medical solution.

Methods: MHB is made with purified bovine and porcine collagen, elastin and heparin powders dissolved/mixed in 50°C acidic aqueous solution that reproducibly self-form into a coacervate (Fig 1 thermoplastic gel). The coacervate is melted, homogenized, reformed into thin wafers, cured, cut into particles, sterilized in saline, aseptically syringe filled, and injection force/rheometry measured with a Lloyd Force Tester. In a GLP-CRO study that included maximum synovial fluid aspiration to maximize particle injection volume, ~0.5cc particles were injected into 12 rabbit stifle joints (six 3-4Kg New Zealand Whites) observed for wellness, motion and histology by a CRO pathologist at 1 & 4wks. Additionally, in companion canine case studies, various breeds were injected with particles to fill the synovial space 60-75% into elbow, stifle, and hip joints with severe radiographic OA, poor behavior, motion and gait.

Figure 1: manufacturing in small-large batch formats

Results: Rabbit safety study: Rabbits showed no abnormal scores for range of motion, withdrawal response, or joint actions. Pathologist reported cartilage of femoral-tibia condyles and menisci of all injected stifle joints to be histologically 100% normal, not different from non-injected controls, and integrated test particles at all injected joints. Canine OA case studies: Across five veterinary clinics, great efficacy and safety from injected MHB particles (Kush™) was found in 16 dogs with severe joint OA (radiographic bone spurs & joint degeneration, n=16; Fig 3): Every dog had qualitative enhancements for mobility and energetic behavior (far less sedate). Moreover, each case that was on daily NSAID treatment, which has high likelihood of gastric tract problems developing overtime [3], was discontinued post MHB particles injection (>12 months; see chart below).



Articulating Hyaline Cartilage

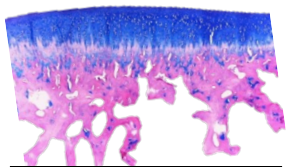


Figure 2: Alcian blue cartilage stain of stifle joint at 4 weeks post-injection

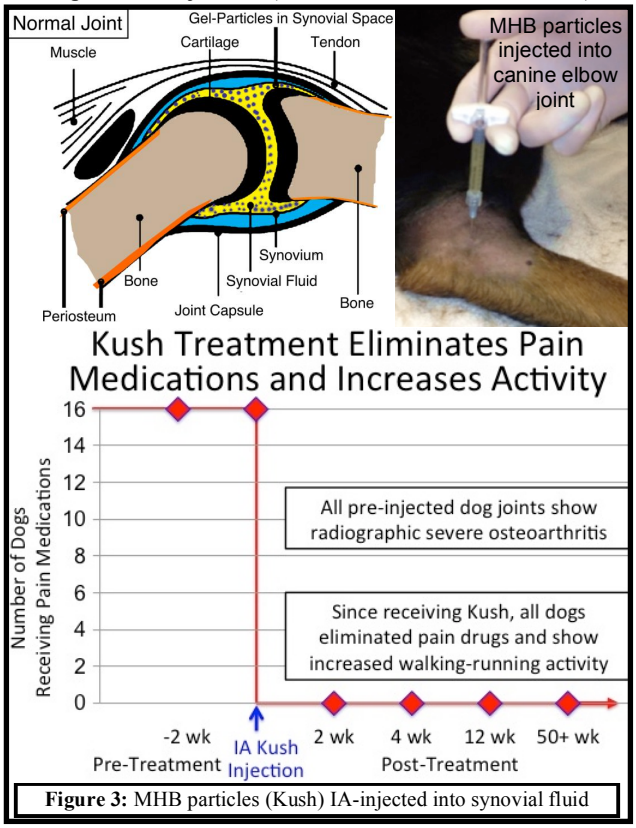


Figure 3: MHB particles (Kush) IA-injected into synovial fluid

Conclusions: MHB particles provide safe cushion and lubricity to the joint, as well as scaffolding that can help natural healing processes rebuild functional tissue. In this way, MHB particles can alleviate pain associated with missing and damaged cartilage, as well as provide a protective environment in much the same way native cartilage protects the joint. MHB is a scaffolding biomaterial that imparts chemical-structural feedback for natural cell-mediated responses, which allows implanted grafts and devices to integrate and/or regenerate endogenous tissues. This biomaterial has been used in a number of tissue applications, including spinal disks, tissue glue, skin (cosmetic dermal filler to correct wrinkles*) [4], urology (urinary sphincter muscle regeneration), blood vessel grafts and more [1,2]. Current treatment for canine OA relies on constant NSAID medication [5]. The data presented here demonstrate successful eradication of NSAID treatment for canine OA pain following injection of MHB particles.
*www.clinicaltrial.gov - NCT00414544

References: [**1**] Masters DB Soc Biomat. Boston'13; #155 [**2**] US Patent #8,153,591 [**3**] Ding C. Inflammation 2002; 26.3;139-142. [**4**] Smith S, Amer Soc Derm Surg; Nov'08 [**5**] Sharkey M; FDA Veterinarian. 2006; XXI