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PEPITEM supports new bone and blood vessel growth in osteoporosis

While bones may appear solid and unchanging, they are a living tissue that is constantly being broken down and rebuilt in a process known as bone remodelling. Specialised cells (called osteoclasts) carefully remove old or damaged bone, while other cells (called osteoblasts) work simultaneously to repair and build new bone. In healthy adults, this cycle is finely balanced, ensuring that bone, through continuous replacement, remains strong and resilient. In fact, most of the human skeleton is replaced with brand new bone roughly every 10 years. However, imbalances in this relationship between osteoblasts and osteoclasts can cause excessive bone loss, leading to diseases such as osteoporosis.

Current treatments for bone loss tend to target one side of the scale, either blocking bone breakdown or briefly promoting bone formation, and often cause unwanted side effects like fractures and pain. Therefore, new treatment approaches are needed that restore bone health and improve the lives of patients who suffer from bone loss.

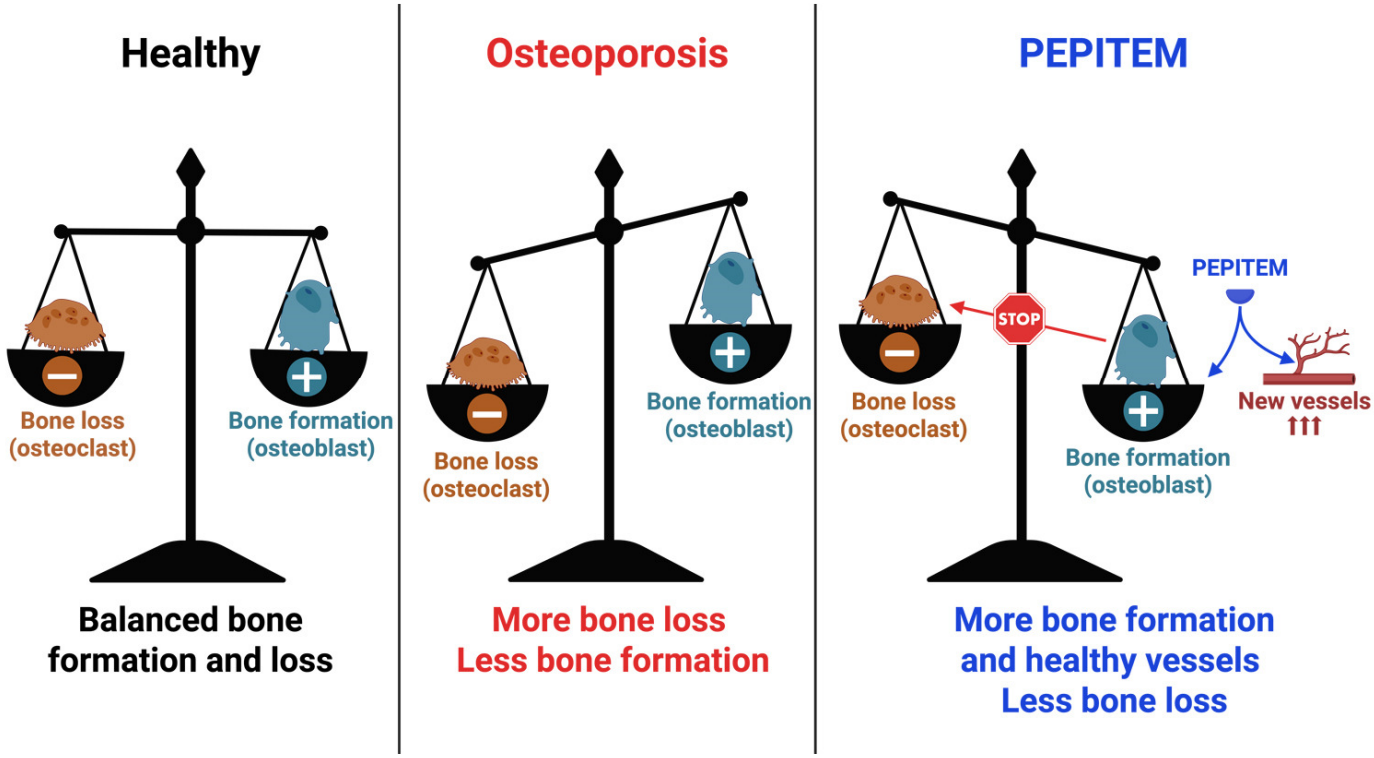

Fig. 1. Healthy bones are maintained by the balance between bone-removing cells (osteoclasts) and bone-building cells (osteoblasts). In osteoporosis, this balance is disrupted, resulting in excessive bone loss and insufficient bone formation, which makes bones brittle. PEPITEM helps to slow bone loss, boost bone repair, and support the growth of healthy blood vessels that nourish bone. Exploring PEPITEM as a therapy for bone disease could target this balance, offering a new way to strengthen bones and restore stability.

Our research focused on a naturally occurring peptide called PEPITEM. This small molecule is made in the body, but its production is reduced as we age. Unlike current therapies, PEPITEM works on both sides of the scale, directly stimulating osteoblasts to build new bone and indirectly limiting excessive osteoclast activity. Significantly, PEPITEM does not entirely block osteoclast activity, allowing bone to be renewed in a manner that mimics the body's natural balance.

In our 2025 study in *Biomedicine & Pharmacotherapy,* we asked how PEPITEM readdresses this balance. To answer this, we tested smaller parts of the peptide, known as bioactive fragments. Some of these smaller fragments encouraged osteoblasts to form more bone, while others limited the formation of new osteoclasts by increasing the production of a natural inhibitor (OPG) made by osteoblasts. In other words, specific fragments direct osteoblasts to act as regulators of osteoclasts, mirroring the body's natural bone remodelling balance. Although some peptide fragments showed promising effects, none were able to reproduce the full impact of PEPITEM. This showed that while different parts of PEPITEM have different roles, the full-length molecule is necessary for maximum benefit (like ingredients versus a whole recipe).

When tested in healthy mice, we found that PEPITEM increased bone volume and improved the microscopic structure of bone. Using a mouse model of postmenopausal osteoporosis (induced by ovary removal, which simulates hormone-driven bone loss), we demonstrated that PEPITEM was able to prevent further bone loss and restore features of healthy bone. Although some of the smaller fragments offered partial protection, the full peptide consistently showed the strongest effect.

In addition, we observed that PEPITEM increased the number of a specific type of bone blood vessels, known as type-H. These vessels play a crucial role in bone health as they support bone growth and repair by delivering nutrients and directing osteoblasts to the correct locations. This suggests that PEPITEM supports bone not only by acting on osteoblasts and osteoclasts, but also by enhancing the blood supply that enables new bone formation.

In summary, our 2025 findings, published in *Biomedicine & Pharmacotherapy*, present PEPITEM as a promising new therapy for osteoporosis. Unlike current treatments, which often work on one process and may cause significant side effects, PEPITEM restores balance by working on both sides of the scale while also promoting healthy blood vessel growth. As it is naturally produced in the body, PEPITEM could offer a safer, more effective treatment that not only slows bone loss, but also actively supports bone repair.

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