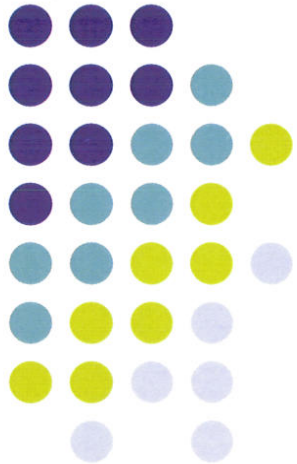
Absorption, distribution, and excretion examinations of 99mTechnetium labelled hyaluronic acid after single dose per oral administration

JULY, 2007



Background

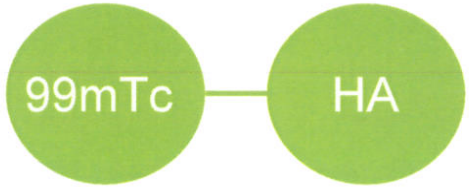
- Hyaluronic acid (HA) is being listed as an ingredient in an ever-increasing number of dietary supplements targeted to joint health and skin health

- No published reports on uptake of HA after oral administration were found in the scientific literature

- The aim of the study:

  To examine the absorption, excretion and distribution of Hyaluronic Acid after a single oral administration

Design of study

- Study group: 

- Control group: 

- Study animals: Wistar rats

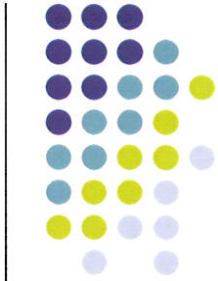
  Beagle dogs

- Sodium hyaluronate
  MW: 1.0-1.5 MDa
- 99mTc: gamma emitting isotope 99mtechnetium (Tc)

Methods

- Tissue biodistribution
- Urinary/faeces excretion examinations
- Blood & urinary clearance
- Scintigraphic examinations
- Nano SPECT/CT scans
- Autoradiography

Results



- HA was labeled with 99mTechnetium at 85% efficiency and was stable for at least 48 hours

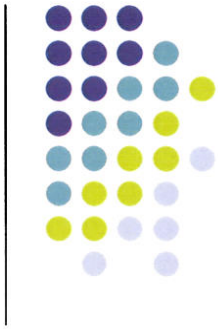
- After a single oral application, a proportion (< 5%) of 99mTc-HA has been absorbed from the gastrointestinal tract

- The absorbed part of 99mTc-HA was distributed to various organs, especially joints and skins. All tissues examined showed incorporation of radioactivity starting at 15 minutes and persisting for 48 hours.

- The main part of applied 99mTc-HA is excreted via the faeces (around 90 % between 0-72 hs) and a small proportion is excreted via the urine (< 5% between 0-72 hs)

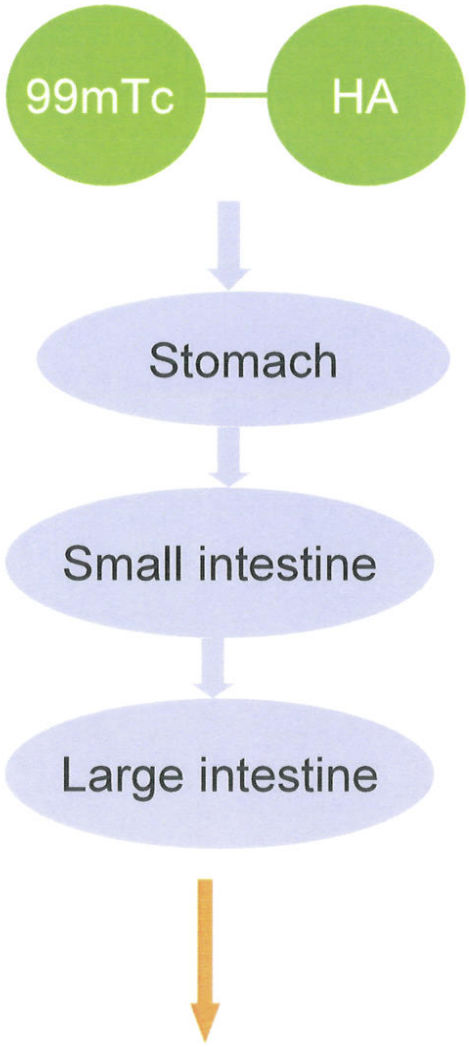
- The control material behave differently – a faster excretion has been seen by the urinary tract from the body

- Scintigraphic imaging, nano SPECT/CT scans, autoradiography in rats have illustrate the presence of labeled HA in joints, connective tissue and skin samples.

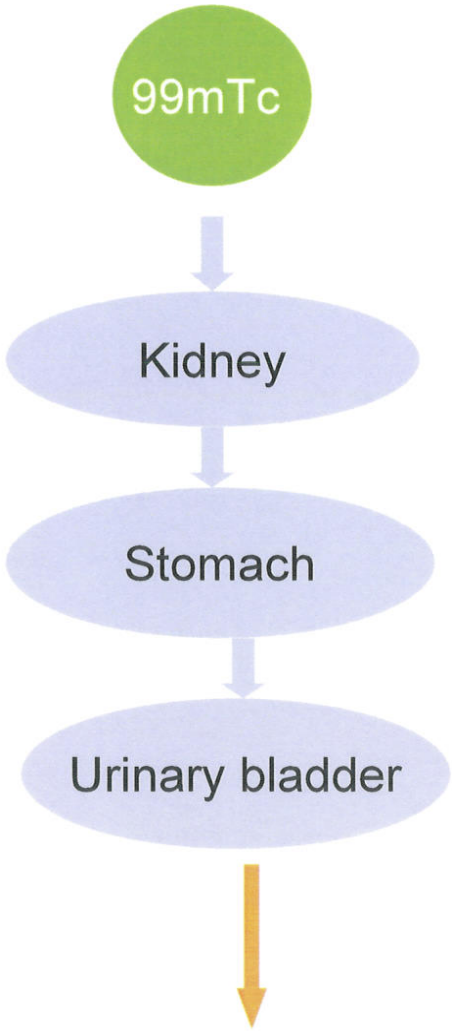


Results in detail

Radioactivity distribution



86.42% excreted by faeces



93.2% excreted by urines

Result

- The control(99mTc) is different from the test study(99mTc-HA) in the radioactivity distribution

- The difference is due to the Sodium hyaluronate

- The metabolism of 99mTc-HA has little connection with free 99mTc

Urinary/faeces excretion in rats

	I.D.% / collected excretums	Average	±	SD
0 – 12 hs	urine	0.34	±	0.11
	faeces	1.84	±	1.58
0 – 24 hs	urine	0.78	±	0.18
	faeces	42.16	±	9.54
0 – 48 hs	urine	1.36	±	0.38
	faeces	69.40	±	9.69
0 – 72 hs	urine	2.04	±	0.63
	faeces	84.62	±	7.79
0 – 72 hs	urine+faeces	86.66	±	8.03

Excretion examinations after per oral application of 99mTc – HA in rats

	I.D.% / collected excretums	Average	±	SD
0 – 12 hs	urine	65. 76	±	3. 71
	faeces	0. 44	±	0. 09
0 – 24 hs	urine	82. 44	±	4. 72
	faeces	0. 64	±	0. 09
0 – 48 hs	urine	88. 96	±	4. 18
	faeces	0. 88	±	0. 08
0 – 72 hs	urine	93. 20	±	4. 45
	faeces	1. 24	±	0. 09
0 – 72 hs	urine+faeces	94. 44	±	4. 51

Excretion examinations after per oral application of 99mTc in rats

Result

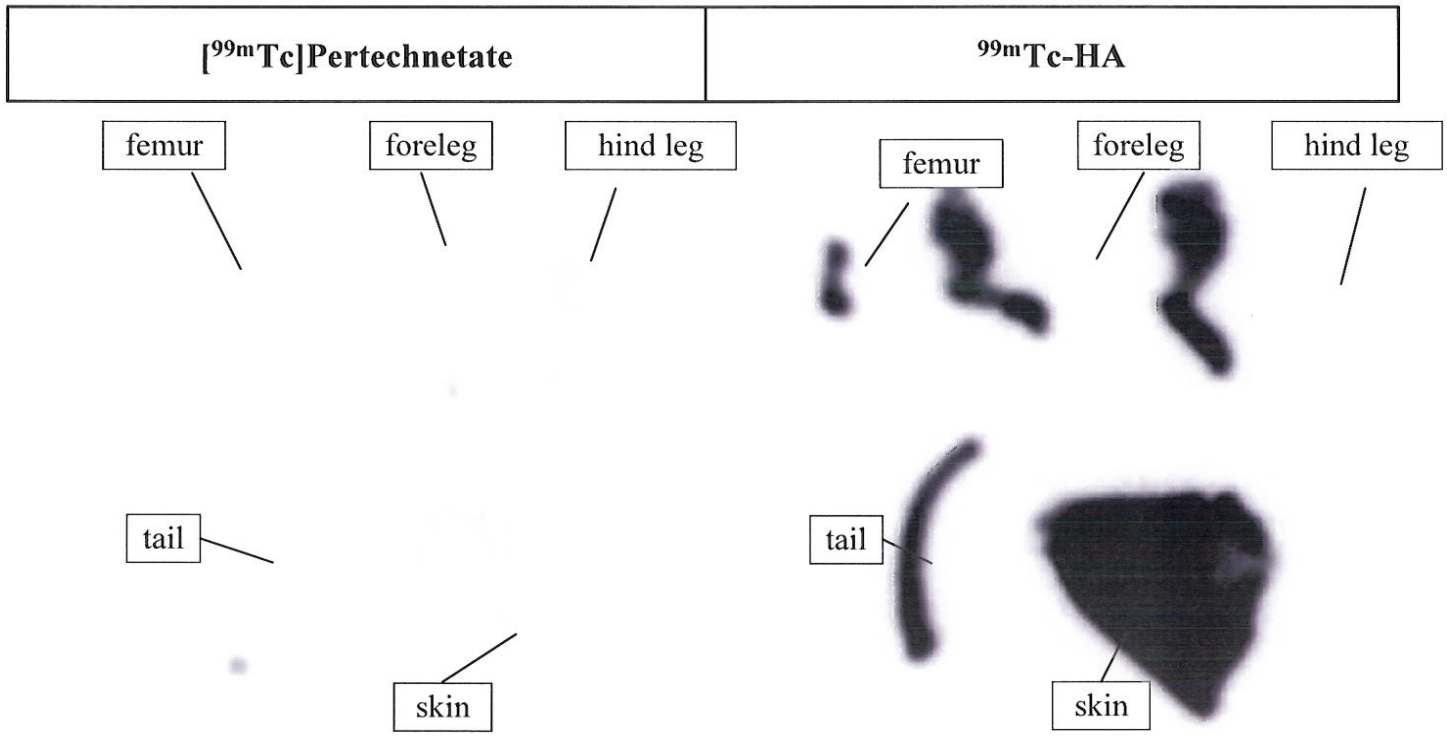
- After 72 hours, recoveries were 84.62+ 7.79% in feces and 2.04 ± 0.63 % in urine, for a total urinary and fecal excretion of 86.66 ± 8.03 % of ingested radioactivity.

- Only 40% of the ingested radioactivity was excreted by 24 hours, most between 12-24 hours

- Approximately 8% of the orally ingested dose of 99mTc-HA had potential for systemic distribution.

The control study turns out that 93.20+ 4.45% of the radioactivity is excreted by urines.

Ex vivoscintigrams of removed targetorgans from 2 rats



Test method: Scintigraphic examinations in Wistar rats

Result

- There are difference of radioactivity distribution between labeled HA and label itself in the joints and skins.

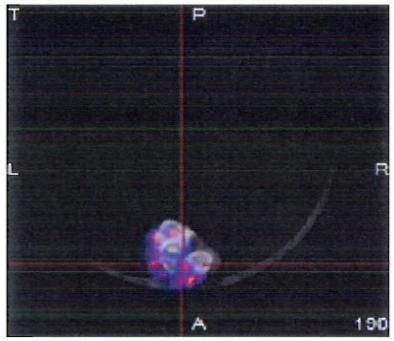
The label(99mTc) is still attached to HA in the body after oral consumption

The radioactivity reached joints and skins is generated by 99mTc-HA instead of free 99mTc

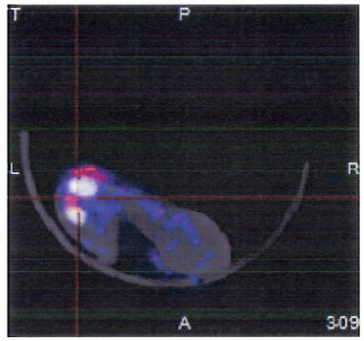
HA gets into joints and skins after oral consumption

Ex vivo images of foreleg, hindleg and femur

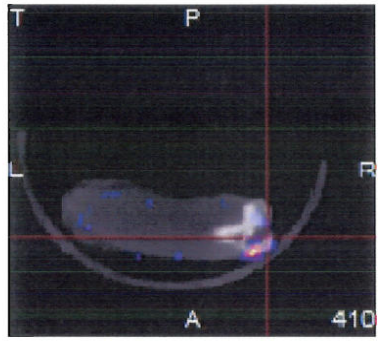
Tarsal joint



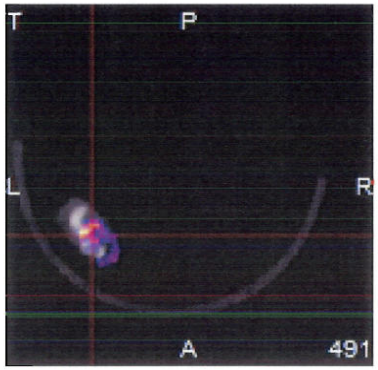
Knee joint



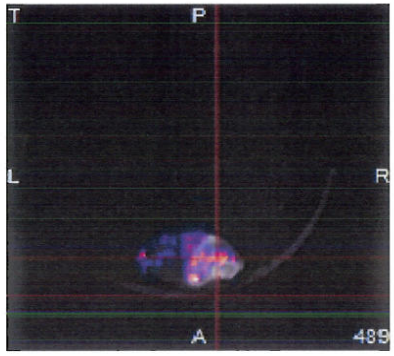
Hip joint



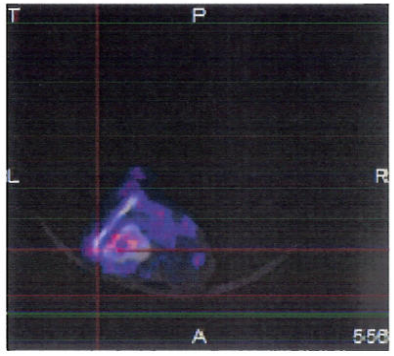
Carpal join



Elbow joint



Shoulder joint

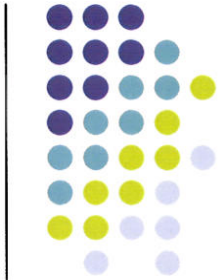


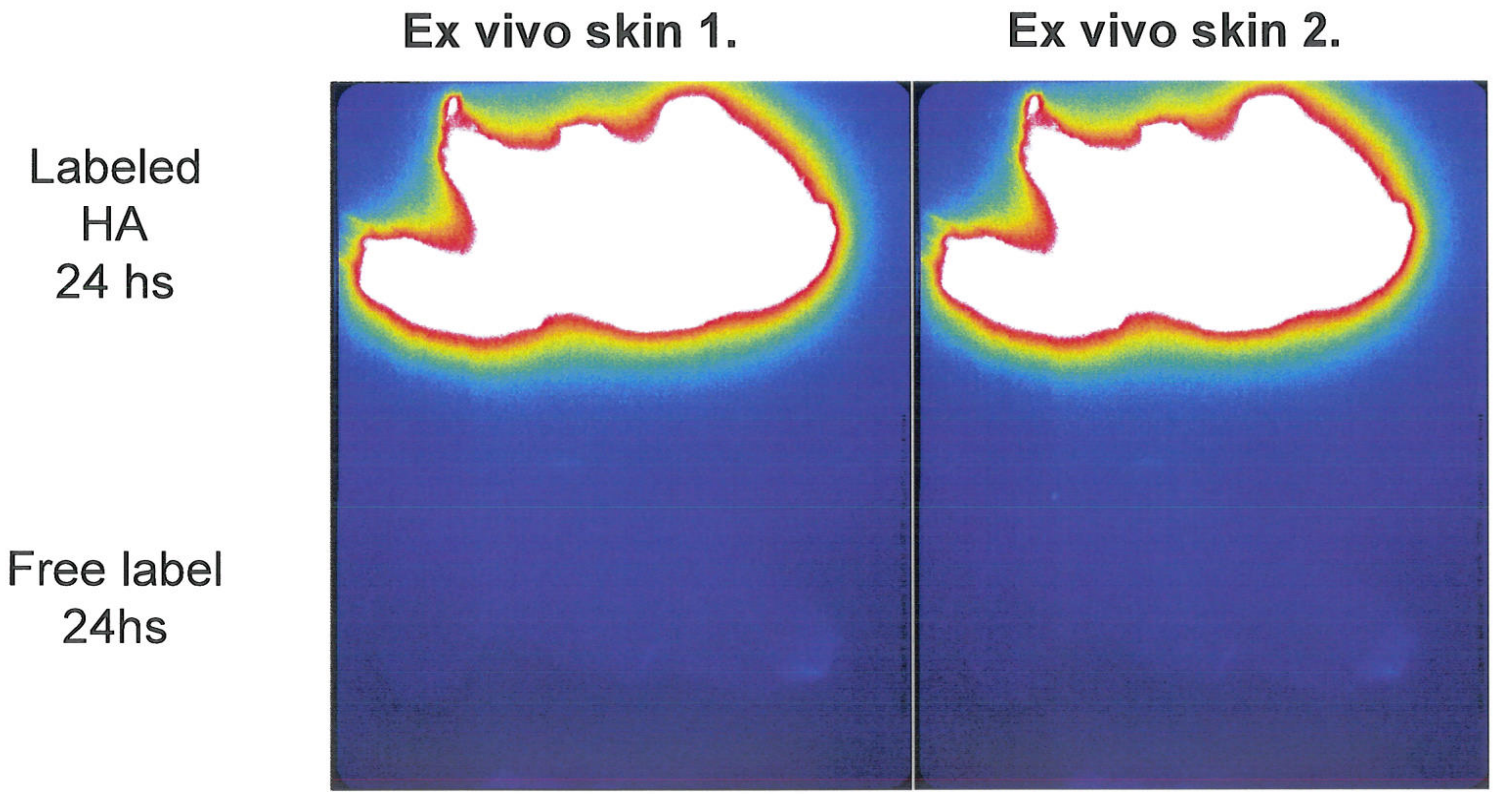
Test method: nano SPECT/CT scans in Wistar rats

Result

- Nano SPECT/CT scans of target organs showed that measurable amounts of radioactivity reached tissues after oral administration of 99mTc-HA, with a special affinity for cartilaginous joints.

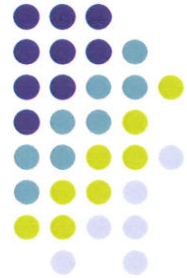
Ex vivo autoradiography of skin 24 hs after application of test and control material





Test method: Autoradiography in Wistar rats

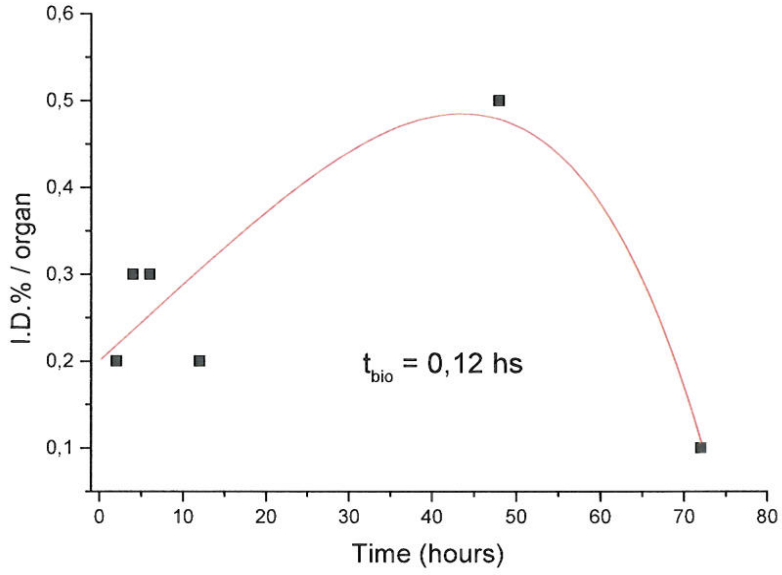
Result



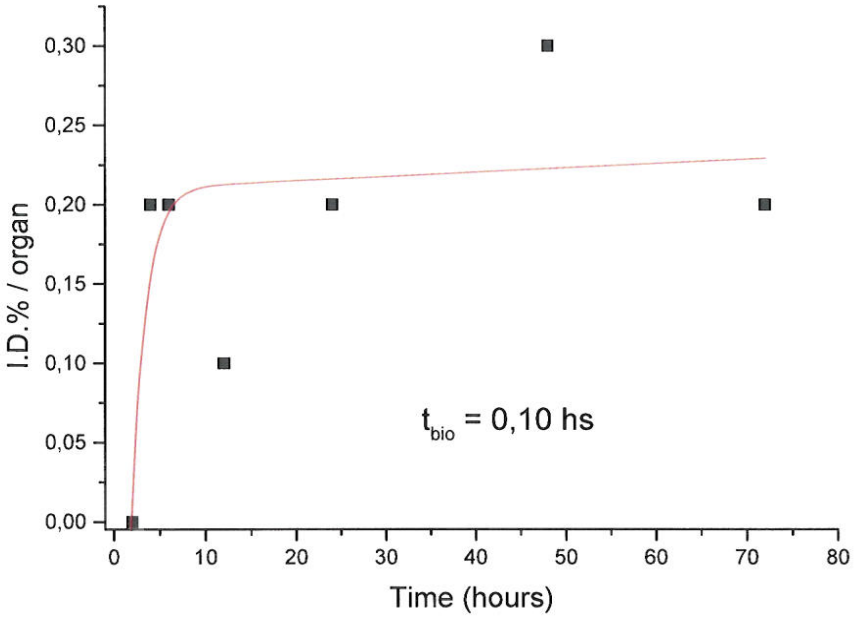
- Autoradiography shows that the radioactivity of 99mTc is still linked with HA

- Measurable amounts of radioactivity reached skins after oral administration of 99mTc-HA

Pharmacokinetic and internal dosimetry of 99mTc-HA

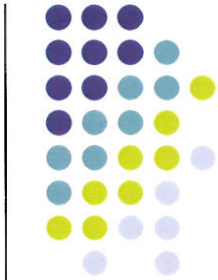


Pharmacokinetic properties of 99mTc-HA in rat knee after oral application



Pharmacokinetic properties of 99mTc-HA in rat skin after oral application

Conclusion



- HA is presented to be the first commercial HA with clinical evidence for uptake and distribution to connective tissues and skins after orally consumption

- The findings support a rationale for biological actions seen in animal and human studies

- The findings support the application of HA in dietary supplements or functional foods designed for joint and skin health.