Introduction

- Angiotensin II (Ang II) is a main effector peptide acting through Angiotensin Type 1 (AT1) receptor.  
- Angiotensin Type 2 (AT2) receptor plays counteractive role to that of AT1 receptor.  
- AT2 receptors are upregulated in myocardial infarction, ischemic injury, atherosclerosis etc. (3)

Fig1 : AT2 receptor

![Fig1](image)

Inhibit cell growth  
Aid apoptosis  
Improved endothelial dysfunction, vasodilation  
Natriuresis  
Modulate ionic currents and channels  
Cardiovascular disorders  
Neurological disorders

Fig2 : Prospective therapeutic applications of AT2 receptor

- Smaller Peptides like Novokinin, LKP and LGP are agonist for AT2 receptor
  I. Greater selectivity  
  II. Less off target binding  
  III. Short half-life

- Bone drug delivery can be utilized for effective therapeutic safety and efficacy
  I. Reduce intrinsic susceptibility of drug to metabolism  
  II. Sustain effective plasma concentration for to exhibit pharmacological activity

Hypothesis

- We hypothesize that chemical coupling of peptide with bone targeting moiety will increase the half life of the peptide.
- We hypothesize that conjugated peptide will have superior therapeutic activity compared to parent peptide owing to its better bioavailability.

Experimental Design

- Synthesize peptides
- Conjugate peptides
- In vitro stability
- In vitro binding
- In vivo PK study
- Compare half-life
- Suitable cell line and signaling studies
- Suitable Animal Model
- Compare efficacy

Fig3: Experimental design flow chart for peptides

Results

- An HPLC method has been developed for detection and purification of the peptides.
- Carried out synthesis of peptides.
- Conjugated the peptides with the bone targeting moiety.

![Fig4](image)

Detection of Novokin in solution

![Fig5](image)

Detection of LKP peptide in solution

Conclusion

This proposed bone delivery approach can:
- Improve bioavailability of peptides.
- Sustain plasma drug concentration.
- Utilize the untapped benefit of smaller peptides more efficiently with less toxic effect.

References


Pocatello | Idaho Falls | Meridian | Twin Falls