

**Supporting Table 2. The close similarity of Angiotensin (1-7), AVE 0991, 20E and estradiol effects.**

Effect	Angiotensin 1-7 (or ACE2 stimulation)	AVE 0991 (non-peptidic Mas agonist)	20E and/or other ecdysteroids	Estradiol
Anabolic (muscle)	Acuña et al., 2014; Cabello-Verrugio et al., 2015, 2017; Cisternas et al., 2015; Abrego et al., 2016; Morales et al., 2014, 2016		Chermnykh et al., 1988; Syrov, 2000; Tóth et al., 2008; Gorelick-Feldman et al., 2008, 2009, 2010; Lawrence, 2012; Parr et al., 2014	Velders et al., 2012; Tchoukouegno Ngeu, 2013; Parr et al., 2014; Chidi-Ogbolu & Baar, 2019
Fat-reducing / Hypolipidemic	Santos et al., 2012; Andrade et al., 2014; Santos & Andrade, 2014; Schuchard et al., 2015	Singh et al., 2012; Yadav et al., 2013	Syrov et al., 1983; Kizelsztejn et al., 2009; Seidlova-Wuttke et al., 2010; Foucault et al., 2012	Seidlova-Wuttke et al., 2010; Lizcano & Guzmán, 2014
Antidiabetic	Liu et al., 2012; Echeverria-Rodriguez et al., 2014; Santos et al., 2014; He et al., 2015; Kilarkaje et al., 2013; Chodavarapu & Lazartigues, 2015; Verma et al., 2012	Singh et al., 2012	Yoshida et al., 1971; Kizelsztejn et al., 2009; Sundaram et al., 2012a,b	Mauvais-Jarvis, 2011; Zhang et al., 2015;
Anti-fibrotic	Lubel et al., 2009, Simões e Silva et al., 2013; Barroso et al., 2015; Willey et al., 2016	Phua et al., 2009	Hung et al., 2012	Wu et al., 2009
Anti-inflammatory	Da Silveira et al., 2010; El-Hashim et al., 2012; Simões e Silva et al., 2013; Barroso et al., 2015; Xue et al., 2019	Da Silvera et al., 2010; Jawien et al., 2012; Skiba et al., 2017	Kurmukov & Syrov, 1988; Xia et al., 2016; Fang et al., 2017; Song et al., 2019	Pedersen et al., 2016; Pelekanou et al., 2016
Neuroprotective	Jiang et al., 2013; Regenhardt et al., 2013; Zheng et al., 2014; Bennion et al., 2015; Villalobos et al., 2016	Lee et al., 2015; Jiang et al., 2018; Mo et al., 2019	Luo et al., 2009; Liu et al., 2011; Hu et al., 2012	Raz et al., 2008; Lebesgue et al., 2010; Arevalo et al., 2015
Cardioprotective	Tallant et al., 2005; Benter et al., 2007; Hao et al., 2015; Tesanovic et al., 2010.	Ferreira et al., 2007; Ebermann et al., 2008; He et al., 2010; Zeng et al., 2012; Cunha et al., 2013; Yadav et al., 2013; Ma et al., 2016	Kurmukov & Ermishina, 1991; Korkach et al., 2007; Xia et al., 2013a	Cong et al., 2013, 2014
Vasorelaxant	Dos Santos & Sampaio, 2015; Raffai et al., 2011; Tesanovic et al., 2010	Lemos et al., 2005		Zhou et al., 2013; Hermenegildo et al., 2011; Sobrino et al., 2010, 2017.
Hematopoïesis stimulation	Rodgers & di Zerega, 2013; Rodgers et al., 2013		Syrov et al., 1997	Nakada et al., 2014
Liver protective	Lubel et al., 2009; Pereira et al., 2007; Li, 2013	Suski et al., 2012	Shakhmurova et al., 2010a; Xia et al., 2013b	Tian et al., 2012
Lung protective	Imai et al., 2008; Klein et al., 2013; Uhal et al., 2013; Shenoy et al., 2015; Cao et al., 2019	Klein et al., 2013; Rodrigues-Machado et al., 2013; Cao et al., 2019	Wu et al., 1998; Li et al., 2013; Xia et al., 2016; Song et al., 2019	Hamidi et al., 2011; Breithaupt-Faloppa et al., 2013
Kidney protective	Zhou et al., 2012; Xu et al., 2013;	Barroso et al., 2012; Suski et al., 2013; Silveira et al., 2010, 2013; Pinheiro et al., 2004.	Syrov et al., 1992; Zou et al., 2010; Hung et al., 2012	Iran-Nejad et al., 2015; Wu et al., 2016
Gastric protective	Zhu et al., 2014; Pawlik et al., 2016	Pawlik et al., 2016	Shakhmurova et al., 2010b; Zhou et al., 2010	Du et al., 2010; Liu et al., 2010
Bone protective	Krishnan et al., 2013		Gao et al., 2008; Kapur et al., 2010; Seidlova-Wuttke et al., 2010b; Dai et al., 2015	Seidlova-Wuttke et al., 2010b
Bone protective	Krishnan et al., 2013		Gao et al., 2008; Kapur et al., 2010; Seidlova-Wuttke et al., 2010b; Dai et al., 2015	Seidlova-Wuttke et al., 2010b

## References for supporting Table 2

- 808  
809  
810 Abrigo J, Simon F, Cabrera D, Cabello-Verrugio C 2016 Angiotensin-(1-7) prevents skeletal muscle atrophy induced  
811 by Transforming Growth Factor type beta (TGF- $\beta$ ) via Mas receptor activation. *Cell Physiol Biochem* **40** 27-38.
- 812 Acuña MJ, Pessina P, Olguin H, Cabrera D, Vio CP, Bader M, Muñoz-Canoves P, Santos RAS, Cabello-Verrugio C,  
813 Brandan E. 2014 Restoration of muscle strength in dystrophic muscle by angiotensin-1-7 through inhibition of  
814 TGF- $\beta$  signalling. *Human Molecular Genetics* **23** (5) 1237-1249.
- 815 Andrade JMO, Paraíso AF, Garcia ZM, Ferreira AVM, Sinisterra RDM, Sousa FB, Guimarães ALS, de Paula AMB,  
816 Campagnole-Santos MJ, Santos RAS *et al.* 2014 Cross-talk between angiotensin-(1-7)/Mas axis and sirtuins in  
817 adipose tissue and metabolism of high-fat feed mice. *Peptides* **55** 158-165.
- 818 Arevalo MA, Azcoitia I, Garcia-Segura LM 2015 The neuroprotective actions of oestradiol and oestrogen receptors.  
819 *Nature reviews Neuroscience* **16** 17-29.
- 820 Barroso LC, Silveira KD, Lima CX, Borges V, Bader M, Rachid M, Santos RAS, Souza DG, Simões e Silva AC,  
821 Teixeira MM 2012 Renoprotective effects of AVE0991, a nonpeptide Mas receptor agonist, in experimental acute  
822 renal injury. *Int J Hypertension* **2012**, Article ID 808726, doi:10.1155/2012/808726.
- 823 Barroso LC, Silveira KD, Teixeira MM, Simões Silva AC 2015 Mas and inflammation. In: The protective arm of the  
824 Renin-Angiotensin System (RAS), pp. 213-217. Eds Unger T, Steckelings UM, dos Santos RAS. Amsterdam.  
825 Academic Press Publications.
- 826 Bennion DM, Regenhardt RW, Mecca AP, Sumners C 2015 Mas and neuroprotection in stroke. In: The protective  
827 arm of the Renin-Angiotensin System (RAS), pp. 201-205. Eds Unger T, Steckelings UM, dos Santos RAS.  
828 Amsterdam. Academic Press Publications.
- 829 Benter IF, Yousif MHM, Cojocel C, Al-Maghrebi M, Diz DI 2007 Angiotensin-(1-7) prevents diabetes-induced  
830 cardiovascular dysfunction. *Am J Physiol Heart Circ Physiol* **292** 11666-11672.
- 831 Breithaupt-Faloppa AC, Fantozzi ET, de Assis Ramos MM, Vitoretti LB, Couto GK, Lino-dos-Santos-Franco A,  
832 Rossoni LV, Oliveira-Filho RM, Vargaftig BB, Tavares-de-Lima VV 2013 Protective effect of estradiol on acute  
833 lung inflammation induced by an intestinal ischemic insult is dependent of nitric oxide. *Shock* **40(3)** 203-209.
- 834 Cabello-Verrugio C, Morales MG, Rivera JC, Cabrera D, Simon F 2015 Renin-Angiotensin System: an old player  
835 with novel functions. *Med Res Rev* **35(3)** 437-463.
- 836 Cabello-Verrugio C, Rivera JC, Garcia D 2017 Skeletal muscle wasting: new role of nonclassical renin-angiotensin  
837 system. *Curr Opin Clin Nutr Metab Care* **20(3)** 158-163.
- 838 Cao Y, Liu Y, Shang J, Yuan Z, Ping F, Yao S, Guo Y, Li Y. 2019 Ang-(1-7) treatment attenuates lipopolysaccharide-  
839 induced early pulmonary fibrosis. *Laboratory Investigation* **99 (12)** 1770-1783.
- 840 Chermnykh NS, Shimanovsky NL, Shutko GV, Syrov VN 1988 Effects of methandrostenolone and ecdysterone on  
841 physical endurance of animals and protein metabolism in the skeletal muscles. *Farmakol Toksikol* **6** 57-62.
- 842 Chidi-Ogbolu N, Baar K 2019 Effect of estrogen on musculoskeletal performance and injury risk. *Frontiers in*  
843 *Physiology* **9** article 1834.
- 844 Chodavarapu H, Lazartigues E 2015 ACE2 and glycemic control. In: The protective arm of the Renin-Angiotensin  
845 System (RAS), pp. 219-223. Eds Unger T, Steckelings UM, dos Santos RAS. Amsterdam. Academic Press  
846 Publications.
- 847 Cisternas F, Morales MG, Meneses C, Simon F, Brandan E, Abroggi J, Vazquez V, Cabello-Verrugio C 2015  
848 Angiotensin-(1-7) decreases skeletal muscle atrophy induced by angiotensin II through a Mas receptor-dependent  
849 mechanism. *Clin Sci* **128** 307-319.
- 850 Cong B, Zhu X, Cao B, Xiao L, Wang Z, Ni X 2013 Estrogens protect myocardium against ischemia/reperfusion insult  
851 by up-regulation of CRH receptor type 2 in female rats. *International Journal of Cardiology* **168** 4755-4760.
- 852 Cong B, Xu Y, Sheng H, Zhu X, Wang L, Zhao W, Tang Z, Lu J, Ni X 2014 Cardioprotection of 17 $\beta$ -estradiol against  
853 hypoxia/reoxygenation in cardiomyocytes is partly through up-regulation of CRH receptor type 2. *Molecular and*  
854 *Cellular Endocrinology* **382** 17-25.
- 855 Cunha TMB, Lima WG, Silva ME, Santos RAS, Campagnole-Santos MJ, Alzamora AC 2013 The nonpeptide ANG-  
856 (1-7) mimic AVE 0991 attenuates cardiac remodeling and improves baroreflex sensitivity in renovascular  
857 hypertensive rats. *Life Sciences* **92** 266-275.
- 858 Dai W, Zhang H, Zhong ZA, Jiang L, Chen H, Lay YA, Kot A, Ritchie RO, Lane NE, Yao W 2015  $\beta$ -Ecdysone  
859 augments peak bone mass in mice of both sexes. *Clin Orthop Relat Res* **473** 2495-2504.

- 860 dos Santos RAS, Sampaio WO 2015 Mas receptor: vascular and blood pressure effects. In: The protective arm of  
861 the Renin-Angiotensin System (RAS), pp. 197-200. Eds Unger T, Steckelings UM, dos Santos RAS. Amsterdam.  
862 Academic Press Publications.
- 863 Du D, Ma X, Zhang J, Zjhang Y, Zhou X, Li Y 2010 Cellular and molecular mechanisms of 17 $\beta$ -estradiol  
864 postconditioning protection against gastric mucosal injury induced by ischemia/reperfusion in rats. *Life Sciences*  
865 **86** 30-38.
- 866 Ebermann L, Spillmann F, Sidiropoulos M, Escher F, Heringer-Walther S, Schultheiss HP, Tschöpe C, Walther T  
867 2008 The angiotensin-(1-7) receptor agonist AVE0991 is cardioprotective in diabetic rats. *Eur J Pharmacol* **590**  
868 276-280.
- 869 Echeverria-Rodríguez O, del Valle-Mondragón L, Hong E 2014 Angiotensin 1-7 improves insulin sensitivity by  
870 increasing skeletal muscle glucose uptake in vivo. *Peptides* **51** 26-30.
- 871 El-Hashim AZ, Renno WM, Raghupathy R, Abduo HT, Akhtar S, Benter IF 2012 Angiotensin-(1-7) inhibits allergic  
872 inflammation, via the MAS1 receptor, through suppression of ERK1/2- and NF-KB-dependent pathways. *Br J*  
873 *Pharmacol* **166** 1964-1976.
- 874 Ferreira AJ, Jacoby BA, Araújo CAA, Macedo FAFF, Silva GAB, Almeida AP, Caliar MV, Santos RAS 2007 The  
875 nonpeptide angiotensin-(1-7) receptor Mas agonist AVE-0991 attenuates heart failure induced by myocardial  
876 infarction. *Am J Physiol Heart Circ Physiol* **292** H1113-H1119.
- 877 Fang L, Li J, Zhou J, Wang X, Guo L 2017 Isolation and purification of three ecdysteroids from the stems of *Diploclisia*  
878 *glaucescens* by high-speed countercurrent chromatography and their anti-inflammatory activities in vitro.  
879 *Molecules* **22** 1310. Doi:10.3390/molecules22081310.
- 880 Foucault AS, Mathé V, Lafont R, Even P, Diah W, Veillet S, Tomé D, Huneau D, Hermier D, Quignard-Boulangé A  
881 2012 Quinoa extract enriched in 20-hydroxyecdysone protects mice from diet-induced obesity and modulates  
882 adipokines expression. *Obesity* **20** 270-277.
- 883 Gao L, Cai G, Shi X 2008  $\beta$ -Ecdysterone induces osteogenic differentiation in mouse mesenchymal stem cells and  
884 relieves osteoporosis. *Biol Pharm Bull* **31(12)** 2245-2249.
- 885 Gorelick-Feldman JI 2009 Phytoecdysteroids: understanding their anabolic activity. PhD Thesis, Rutgers University.  
886 Available at <https://rucore.libraries.rutgers.edu/rutgers-lib/25806/>
- 887 Gorelick-Feldman J, MacLean D, Ilic N, Poulev A, Lila MA, Cheng D, Raskin I 2008 Phytoecdysteroids increase  
888 protein synthesis in skeletal muscle cells. *J Agric Food Chem* **56** 3532-3537.
- 889 Gorelick-Feldman J, Cohick W, Raskin I 2010 Ecdysteroids elicit a rapid Ca<sup>2+</sup> flux leading to Akt activation and  
890 increased protein synthesis in skeletal muscle cells. *Steroids*, **70** 632-637.
- 891 Hamidi SA, Dickman KG, Berisha H, Said SI 2011 17 $\beta$ -Estradiol protects the lung against acute injury: possible  
892 mediation by the Vasoactive Intestinal Polypeptide. *Endocrinology* **152(12)** 4729-4737.
- 893 Hao P, Yang J, Liu Y, Zhang M, Zhang K, Gao F, Chen Y, Zhang C, Zhang Y 2015 Combination of angiotensin-(1-  
894 7) with perindopril is better than single therapy in ameliorating diabetic cardiomyopathy. *Scientific Reports* **5** 8794.  
895 DOI : 10.1038/srep08794.
- 896 He JG, Chen SL, Huang YY, Chen YL, Dong YG, Ma H 2010 The nonpeptide AVE0991 attenuates myocardial  
897 hypertrophy as induced by angiotensin II through downregulation of transforming growth factor- $\beta$ 1/Smad2  
898 expression. *Heart Vessels* **25(5)** 438-443.
- 899 He J, Yang Z, Yang H, Wang L, Wu H, Fan Y, Wang W, Fan X, Li X 2015 Regulation of insulin sensitivity, insulin  
900 production, and pancreatic  $\beta$  cell survival by angiotensin-(1-7) in a rat model of streptozotocin-induced diabetes  
901 mellitus. *Peptides* **64** 49-54.
- 902 Hermenegildo C, Sobrino A, Monsalve E, Bueno-Beti C, Laguna-Fernández AL, Sánchez-Ferrer CF, Peiró C, Novella  
903 S. 2011 Estradiol-induced nitric oxide production and vascular relaxation are mediated through angiotensin 1-7  
904 mas receptor. *Journal of Hypertension* **29** p e63.
- 905 Hu J, Luo CX, Chu WH, Shan YA, Qian ZM, Zhu G, Yu YB, Feng H 2012 20-Hydroxyecdysone protects against  
906 oxidative stress-induced neuronal injury by scavenging free radicals and modulating NF- $\kappa$ B and JNK pathways.  
907 *PLoS ONE* **7(12)** e50764.
- 908 Hung TJ, Chen WM, Liu SF, Liao TN, Lee TC, Chuang LY, Guh JY, Hung CY, Hung HJ, Chen PY *et al.* 2012 20-  
909 Hydroxyecdysone attenuates TGF- $\beta$ 1-induced renal cellular fibrosis in proximal tubule cells. *J Diabetes*  
910 *Complications* **26(6)** 463-469.
- 911 Imai Y, Kuba K, Penninger JM 2008 The discovery of angiotensin-converting enzyme 2 and its role in acute lung  
912 injury in mice. *Exp Physiol* **93(5)** 543-548.
- 913 Iran-Nejad A, Nematbakhsh M, Eshraghi-Jazi F, Talebi A 2015 Protective role of estradiol on kidney injury induced  
914 by renal ischemia-reperfusion in male and female rats. *International Journal of Preventive Medicine* **6** 22.

- 915 Jawien J, Toton-Zuranska J, Kus K, Pawlowska M, Olszanecki R, Korbut R 2012 The effect of AVE 0991, nebivolol  
916 and doxycycline on inflammatory mediators in an apoE-*knockout* mouse model of atherosclerosis. *Med Sci Monit*  
917 **18(10)** BR389-393.
- 918 Jiang T, Gao L, Shi J, Lu J, Wang Y, Zhang Y 2013 Angiotensin-(1-7) modulates reini-angiotensin system associated  
919 with reducing oxidative stress and attenuating neuronal apoptosis in the brain of hypertensive rats. *Pharmacol*  
920 *Res* **67** 84-93.
- 921 Jiang T, Xue LJ, Yang Y, Wang QG, Xue X, Ou Z, Gao Q, Shi JQ, Wu L, Zhang YD 2018 AVE0991, a nonpeptide  
922 analogue of Ang-(1-7), attenuates aging-related neuroinflammation. *Aging* **10 (4)** 645-657.
- 923 Kapur P, Wuttke W, Jarry H, Seidlova-Wuttke D 2010 Beneficial effects of  $\beta$ -ecdysone on the joint, epiphyseal  
924 cartilage tissue and trabecular bone in ovariectomized rats. *Phytomedicine* **17** 350-355.
- 925 Kilarkaje N, Yousif MHM, El-Hashim AZ, Makki B, Akhtar S, Benter IF. 2013 Role of angiotensin II and angiotensin-  
926 (1-7) in diabetes-induced oxidative DNA damage in the corpus cavernosum. *Fertil Steril* **100** 226-233.
- 927 Kizelsztejn P, Govorko D, Komarnytsky S, Evans A, Wang Z, Cefalu WT, Raskin I 2009 20-Hydroxyecdysone  
928 decreases weight and hyperglycemia in a diet-induced obesity mice model. *Am J Physiol Endocrinol Metab* **296**  
929 E433-E439.
- 930 Klein N, Gembardt F, Supé S, Kaestle SM, Nickles H, Erfinanda L, Lei X, Yin J, Wang L, Mertens M, et al. 2013  
931 Angiotensin-(1-7) protects from experimental acute lung injury. *Critical Care Medicine* **41(11)** e334-e343.
- 932 Korkach YuP, Kotsiuruba AV, Psryslazhna OD, Mohyl'nyts'ka LD, Sahach VF 2007 NO-dependent mechanisms of  
933 ecdysterone protective action on the heart and vessels in streptozotocin-induced diabetes mellitus in rats. *Fiziol*  
934 *Zh* **53(3)** 3-8.
- 935 Krishnan B, Smith TL, Dubey P, Zapadka ME, Torti FM, Willingham MC, Tallant EA, Gallagher PE 2013 Angiotensin-  
936 (1-7) attenuates metastatic prostate cancer and reduces osteoclastogenesis. *Prostate* **73** 71-82.
- 937 Kurmukov AG, Ermishina OA 1991 The effect of ecdysterone on experimental arrhythmias and changes in the  
938 hemodynamics and myocardial contractility induced by coronary artery occlusion. *Farmakologiya i Toksikologiya*  
939 **54(1)** 27-29.
- 940 Kurmukov AG, Syrov VN 1988 Anti-inflammatory properties of ecdysterone. *Meditinskii Zhurnal Uzbekistana* **10** 68-  
941 70.
- 942 Lautner RQ, Villela DC, Fraga-Silva RA, Silva N, Verano-Braga T, Costa-Fraga F, Jankowski J, Jankowski V, Sousa  
943 F, Alzamora A *et al.* 2013 Discovery and characterization of alamandine, a novel component of the renin-  
944 angiotensin system. *Circulation Res* **112(8)** 1104-1111.
- 945 Lawrence MM 2012 *Ajuga turkestanica* as a countermeasure against sarcopenia and dynapenia. Ms thesis,  
946 Appalachian State University.
- 947 Lebesgue D, Traub M, De Butte-Smith M, Chen C, Zukin RS, Kelly MJ, Etgen AM 2010 Acute administration of non-  
948 classical estrogen receptor agonists attenuates ischemia-induced hippocampal neural loss in middle-aged female  
949 rats. *PLoS ONE* **5(1)** e8642.
- 950 Lee S, Evans MA, Chu HX, Kim HA, Widdop RE, Drummond GR, Sobey C 2015 Effect of a selective Mas receptor  
951 agonist in cerebral ischemia in vitro and in vivo. *PLoS ONE* **10(11)** e0142087.
- 952 Lemos VS, Silva DM, Walther T, Alenina N, Bader M, Santos RA 2005 The endothelium-dependent vasodilator effect  
953 of the nonpeptide Ang(1-7) mimic AVE 0991 is abolished in the aorta of mas-knockout mice. *J Cardiovasc*  
954 *Pharmacol* **46(3)** 274-279.
- 955 Li J, Wu X, Zhang J, Wu X, Gao D, Shen T, Gu C. 2013 Effect of ecdysterone on the expression of toll-like receptor  
956 4 and surfactant protein A in lung tissue of rats with acute lung injury. *Infect Inflamm Rep* **14(1)** 22-26.
- 957 Li X 2013 Up-regulation of the angiotensin-converting enzyme 2/angiotensin-(1-7)/Mas axis protects against liver  
958 fibrosis by inhibiting Nox4/Smad3 pathway in bile-duct-ligation rats. *J Hepatol* **58** S457.
- 959 Liu C, Lv XH, Li HX, Cao X, Zhang F, Wang L, Yu M, Yang JK 2012 Angiotensin-(1-7) suppresses oxidative stress  
960 and improves glucose uptake via Mas receptor in adipocytes. *Acta Diabetol* **49** 291-299.
- 961 Liu Z, Chen Y, Chen Z, Tang W, Zhu G, Wang X, Feng H 2011 Effect of ecdysterone on the nervous lesions of  
962 rabbits acquired after subarachnoid hemorrhage. *Medical Journal of Chinese People's Liberation Army*, **36(12)**  
963 1351-1353.
- 964 Lizcano F, Guzmán G 2014 Estrogen Deficiency and the Origin of Obesity during Menopause. *Biomed Res Int* 2014:  
965 757461.
- 966 Lubel JS, Herath CB, Tchongue J, Grace J, Jia Z, Spencer K, Casley D, Crowley P, Sievert W, Burrell LM, Angus  
967 PW 2009 Angiotensin-(1-7), an alternative metabolite of the renin-angiotensin system, is up-regulated in human  
968 liver disease and has antifibrotic activity in the bile-duct-ligated rat. *Clin Sci* **117** 375-386.

- 969 Luo H, Luo C, Zhang Y, Chi L, Li L, Chen K 2009 Effect of ecdysterone on injury of lipid peroxidation following focal  
970 cerebral ischemia in rats. *Zhongguo Yaoye* **18(15)** 12-14.
- 971 Ma Y, Huang H, Jiang J, Wu L, Lin C, Tang A, Dai G, He J, Chen Y 2016 AVE 0991 attenuates cardiac hypertrophy  
972 through reducing oxidative stress. *Biochem Biophys Res Commun* **474** 621-625.
- 973 Mauvais-Jarvis F 2011 Estrogen and androgen receptors: regulators of fuel homeostasis and emerging targets for  
974 diabetes and obesity. *Trends Endocr Metab* **22(1)** 24-33.
- 975 Mo J, Enkhjargal B, Travis ZD, Zhou K, Wu P, Zhang G, Zhu Q, Zhang T, Peng J, Xu W *et al.* 2019 AVE0991  
976 attenuates oxidative stress and neuronal apoptosis via Mas/PKA/CREB/UCP-2 pathway after subarachnoid  
977 hemorrhage in rats. *Redox Biology* **20** 75-86.
- 978 Morales MG, Abrigo J, Meneses C, Simon F, Cisternas F, Rivera AC, Vazquez Y, Cabello-Verrugio C 2014 The Ang-  
979 (1-7)/Mas-1 axis attenuates the expression and signalling of TGF- $\beta$ 1 induced by AngII in mouse skeletal muscle.  
980 *Clinical Science* **127** 251-264.
- 981 Morales MG, Abrigo J, Acuña MJ, Santos RA, Bader M, Brandan E, Simon F, Olguin H, Cabrera D, Cabello-Verrugio  
982 C 2016 Angiotensin-(1-7) attenuates disuse skeletal muscle atrophy in mice via its receptor, Mas. *Disease Models  
983 & Mechanisms* **9** 441-449.
- 984 Nakada D, Oguro H, Levi BP, Ryan N, Kitano A, Saitoh Y, Takeichi M, Wendt GR, Morrison SJ 2014 Estrogen  
985 increases haematopoietic stem cell self-renewal in females and during pregnancy. *Nature* **505(7484)** 555-558.
- 986 Parr MK, Zhao P, Haupt O, Tchoukouegno Ngueu S, Hengevoss J, Fritzemeier KH, Piechotta M, Schlörer N, Muhn  
987 P, Zheng WY *et al.* 2014 Estrogen receptor beta is involved in skeletal muscle hypertrophy induced by the  
988 phytoecdysteroid ecdysterone. *Mol Nutr Food Res* **58** 1861-1872.
- 989 Parr MK, Botré F, Naß A, Hengevoss J, Diel P, Wolber G 2015 Ecdysteroids: a novel class of anabolic agents? *Biol  
990 Sport* **32** 169-173.
- 991 Pawlik MW, Kwiecien S, Ptak-Belowska A, Pajdo R, Olszanecki R, Suski M, Madej J, Targosz A, Konturek SJ, Korbut  
992 R *et al.* 2016 The renin-angiotensin system and its vasoactive metabolite angiotensin-(1-7) in the mechanism of  
993 the healing of preexisting gastric ulcers. The involvement of Mas receptors, nitric oxide, prostaglandins and  
994 proinflammatory cytokines. *Journal of Physiology and Pharmacology* **67(1)** 75-91.
- 995 Pedersen AL, Nelson LH, Saldanha CJ 2016 Centrally synthesized estradiol is a potent anti-inflammatory in the  
996 injured Zebra finch brain. *Endocrinology* **157** 2041-2051.
- 997 Pelekanou V, Kampa M, Kiagiadaki F, Deli A, Theodoropoulos P, Agrogiannis G, Patsouris E, Tsapis A, Castanas  
998 E, Notas G 2016 Estrogen anti-inflammatory activity on human monocytes is mediated through cross-talk  
999 between estrogen receptor ER $\alpha$ 36 and GPR30/GPER1. *J Leukoc Biol* **99** 333-347.
- 1000 Pereira RM, dos Santos AS, Teixeira MM, Leite VHR, Costa LP, da Costa Dias FL, Barcelos LS, Collares GB,  
1001 Simões e Silva AC 2007 The renin-angiotensin system in a rat model of hepatic fibrosis: evidence for a protective  
1002 role of angiotensin-(1-7). *J Hepatol* **46** 674-681.
- 1003 Phua DS, Jones ES, Widdop RE 2009 Cardiac anti-fibrotic effects of angiotensin (1-7) effects of angiotensin (1-7)  
1004 mimetic in aged mice. *Hypertension* **53** 1116-1117.
- 1005 Pinheiro SVB, Simões e Silva AC, Sampaio WO, de Paula RD, Mendes EP, Bontempo ED, Pesquero JB, Walther  
1006 T, Alenina N, Bader M *et al.* 2004 Nonpeptide AVE 0991 is an angiotensin-(1-7) receptor Mas agonist in the  
1007 mouse kidney. *Hypertension* **44** 490-496.
- 1008 Raffai G, Durand MJ, Lombard JH 2011 Acute and chronic angiotensin-(1-7) restores vasodilation and reduces  
1009 oxidative stress in mesenteric arteries of salt-fed rats. *Am J Physiol Heart Circ Physiol* **301** H1341-H1352.
- 1010 Raz L, Khan MM, Mahesh VB, Vadlamudi RK, Brann DW 2008 Rapid estrogen signaling in the brain. *Neurosignals*  
1011 **16** 140-153.
- 1012 Regenhardt RW, Desland F, Mecca AP, Pioquinto DJ, Afzal A, Mocco J, Sumners C 2013 Anti-inflammatory effects  
1013 of angiotensin-(1-7) in ischemic stroke. *Neuropharmacol* **71** 154-163.
- 1014 Rodgers KE, diZerega GS 2013 Contribution of the local RAS to hematopoietic function: a novel therapeutic target.  
1015 *Front Endocrinol* **4** article 157.
- 1016 Rodgers KE, Espinoza TB, Roda N, Meeks CJ, diZerega GS 2013 Angiotensin-(1-7) synergizes with colony-  
1017 stimulating factors in hematopoietic recovery. *Cancer Chemother Pharmacol* **72(6)** 1235-1245.
- 1018 Rodrigues-Machado MG, Magalhaes GS, Cardoso JA, Kangussu LM, Murari A, Caliani MV, Oliveira ML, Cara DC,  
1019 Noviello MLM, Marques FD *et al.* 2013 AVE 0991, a non-peptide mimic of angiotensin-(1-7) effects, attenuates  
1020 pulmonary remodelling in a model of chronic asthma. *Br J Pharmacol* **170(4)** 835-846.
- 1021 Santos SHS, Andrade JMO 2014 Angiotensin 1-7: A peptide for preventing and treating metabolic syndrome.  
1022 *Peptides* **59** 34-41.

- 1023 Santos SHS, Giani JF, Burghi V, Miquet JG, Qadri F, Braga JF, Todiras M, Kotnik K, Aleni, a N, Dominici FP *et al.*  
1024 2014 Oral administration of angiotensin-(1-7) ameliorates type 2 diabetes in rats. *J Mol Med* **92** 255-265.
- 1025 Santos SHS, Rodrigues Fernandes L, Santos Pereira C, Senna Guimarães AL, de Paula AMB, Campagnole-Santos  
1026 MJ, Alvarez-Leite JI, Bader M, Santos RAS 2012 Increased circulating angiotensin-(1-7) protects white adipose  
1027 tissue against development of a proinflammatory state stimulated by high-fat diet. *Regulatory Peptides* **178** 64-  
1028 70.
- 1029 Schuchard J, Winkler M, Stölting I, Schuster F, Vogt FM, Barkhausen J, Thorns C, Santos RA, Bader M, Raasch W  
1030 2015 Prevention of weight gain after AT1 receptor blockade in diet-induced rat obesity is at least partially related  
1031 to an angiotensin(1-7)/Mas-dependent mechanism. *Br J Pharmacol* **172(15)** 3764-3778.
- 1032 Seidlova-Wuttke D, Ehrhardt C, Wuttke W 2010a Metabolic effects of 20-OH-ecdysone in ovariectomized rats. *J*  
1033 *Steroid Biochem Mol Biol* **119** 121-126.
- 1034 Seidlova-Wuttke D, Christel D, Kapur P, Nguyen BT, Jarry H, Wuttke W 2010b  $\beta$ -Ecdysone has bone protective but  
1035 no estrogenic effects in ovariectomized rats. *Phytomedicine* **17** 884-899.
- 1036 Shakhmurova GA, Khushbaktova ZA, Syrov VN 2010a Estimation of hepatoprotective and immunocorrecting effects  
1037 of the sum of phytoecdysteroids from *Silene viridiflora* in experimental animals treated with tetrachlormethan.  
1038 *O'zbekiston Biologiya Jurnal* **5** 16-20.
- 1039 Shakhmurova GA, Syrov VN, Khushbaktova ZA 2010b Immunomodulating and antistress activity of ecdysterone and  
1040 turkesterone under immobilization-induced stress conditions in mice. *Pharm Chem J* **44(1)** 7-9.
- 1041 Shenoy V, Ferreira A, Katovich M, Raizada MK 2015 Angiotensin-Converting Enzyme 2/angiotensin-(1-7)/Mas  
1042 receptor axis : emerging pharmacological target for pulmonary diseases. In: The protective arm of the Renin-  
1043 Angiotensin System (RAS), pp. 269-274. Eds Unger T, Steckelings UM, dos Santos RAS. Amsterdam. Academic  
1044 Press Publications.
- 1045 Silveira KD, Santos RAS, Barroso LC, Lima CX, Teixeira MM, Silva ACSE 2010 The administration of the agonist of  
1046 angiotensin-(1-7), AVE0991, improved inflammation and proteinuria in experimental nephrotic syndrome. *Pediatr*  
1047 *Nephrol* **25(9)** 1795.
- 1048 Silveira KD, Barroso LC, Vieira AT, Cisalpino D, Lima CX, Bader M, Arantes RME, dos Santos RAS, Simões-e-Silva  
1049 AC, Teixeira MM 2013 Beneficial effects of the activation of the angiotensin-(1-7) Mas receptor in a murine model  
1050 of adriamycin-induced nephropathy. *PLoS ONE* **8(6)** e66082.
- 1051 Simões e Siva AC, Silveira KD, Ferreira AJ, Teixeira MM 2013 ACE2, angiotensin-(1-7) and Mas receptor axis in  
1052 inflammation and fibrosis. *Br J Pharmacol* **169** 477-492.
- 1053 Singh K, Sharma K, Singh M, Sharma PL 2012 Possible mechanism of the cardio-renal effects of AVE-0991, a non-  
1054 peptide Mas-receptor agonist, in diabetic rats. *JRAAS* **13(3)** 334-340.
- 1055 Skiba DS, Nosalski R, Mikolajczyk TP, Siedlinski M, Rios FJ, Montezano AC, Jawien J, Olszanzcki R, Korbut R,  
1056 Czesnikiewicz-Guzik M *et al.* 2017 Anti-atherosclerotic effect of the angiotensin 1-7 mimetic AVE0991 is mediated  
1057 by inhibition of perivascular and plaque inflammation in early atherosclerosis. *British Journal of Pharmacology*  
1058 **174** 4055-4069.
- 1059 Sobrino A, Novella S, Monsalve E, Oviedo PJ, Laguna-Fernandez A, Bueno C, Hermenegildo C 2010 Estradiol  
1060 regulates renin-angiotensin system towards nitric oxide production through Mas receptor. *Journal of Hypertension*  
1061 **28e-supplA** p e385.
- 1062 Sobrino A, Vallejo S, Novella S, Lázaro-Franco M, Mompeón A, Bueo-Beti C, Walther T, Sánchez-Ferrer C, Peiró C,  
1063 Hermenegildo C 2017 Mas receptor is involved in the estrogen-receptor induced nitric oxide-dependent  
1064 vasorelaxation. *Biochemical Pharmacology* **129** 67-72.
- 1065 Sundaram R, Naresh R, Shanthi P, Sachdanandam P 2012a Efficacy of 20-OH-ecdysone on hepatic key enzymes  
1066 of carbohydrate metabolism in streptozotocin induced diabetic rats. *Phytomedicine*, **19(8-9)** 725-729.
- 1067 Sundaram R, Naresh R, Shanthi P, Sachdanandam P 2012b Ameliorative effect of 20-OH ecdysone on  
1068 streptozotocin induced oxidative stress and  $\beta$ -cell damage in experimental hyperglycemic rats. *Process Biochem.*  
1069 **47** 2072-2080.
- 1070 Song G, Xia XC, Zhang K, Ma Y, Yu R, Li B, Li M, Yu X, Zhang J, Xue S 2019 Protective effect of 20-hydroxyecdysone  
1071 against lipopolysaccharides-induced acute lung injury in mice. *Journal of Pharmaceutics and Drug Research* **2(3)**  
1072 109-114.
- 1073 Suski M, Olszanecki R, Bujak-Gizycka B, Madej J, Stachowicz A, Korbut R 2012 Influence of angiotensin-(1-7)  
1074 peptidemimetic (AVE 0991) on liver mitoproteome in apoE-knockout mice. *Vascular Pharmacol* **56(5-6)** 384.
- 1075 Suski M, Olszanecki R, Stachowicz A, Madej J, Bujak-Gizycka B, Okoń K, Korbut R 2013 The influence of  
1076 angiotensin-(1-7) Mas receptor agonist (AVE 0991) on mitochondrial proteome in kidneys of apoE knockout mice.  
1077 *Biochim Biophys Acta* **1834** 2463-2469.

- 1078 Syrov VN 2000 Comparative experimental investigations of the anabolic activity of ecdysteroids and steranabols.  
1079 *Pharm Chem Journal* **34(4)**193-197.
- 1080 Syrov, VN, Khushbaktova ZA, Abzalova MKh, Sultanov MB 1983 On the hypolipidemic and antiatherosclerotic action  
1081 of phytoecdysteroids. *Dokl Akad Nauk Uzb SSR* **9** 44-45.
- 1082 Syrov VN, Khushbaktova ZA, Nabiev AN 1992 An experimental study of the hepatoprotective properties of  
1083 phytoecdysteroids and nerobol in carbon tetrachloride - induced liver injury. *Eksp Klin Farmakologiya* **55(3)** 61-  
1084 65.
- 1085 Syrov VN, Nasyrova SS, Khushbaktova ZA 1997 The results of experimental study of phytoecdysteroids as  
1086 erythropoiesis stimulators in laboratory animals. *Eksp Klin Farmakologiya* **60(3)** 41-44.
- 1087 Tallant EA, Ferrario CM, Gallagher PE 2005 Angiotensin-(1-7) inhibits growth of cardiac myocytes through activation  
1088 of the mas receptor. *Am J Physiol Heart Circ Physiol* **289** H1560-H1566.
- 1089 Tchoukouegno Nguen S 2013 Bioactivity of plant secondary metabolites. Estrogenic, cytotoxic and anabolic effects  
1090 on estrogen target organs of an extract of *Erythrinaexelsa* and ecdysterone. PhD Thesis, Univ Cologne.
- 1091 Tesanovic S, Vinh A, Gaspari TA, Casley D, Widdop RE 2010 Vasoprotective and atheroprotective effects of  
1092 angiotensin (1-7) in apolipoprotein E-deficient mice, *Arterioscler Thromb Vasc Biol* **30** 1606-1613.
- 1093 Tian GX, Sun Y, Pang CJ, Tan AH, Gao Y, Zhang HY, Yang XB, Li AX, Mo ZN 2012 Oestradiol is a protective factor  
1094 for non-alcoholic fatty liver disease in healthy men. *Obesity Rev* **13(4)** 381-387.
- 1095 Tóth N, Szabó A, Kacsala P, Héger J, Zádor E 2008 20-Hydroxyecdysone increases fiber size in a muscle-specific  
1096 fashion in rat. *Phytomedicine* **15** 691-698.
- 1097 Uhal BD, Nguyen H, Dang M, Gopallawa I, Jiang J, Dang V, Ono S, Morimoto K 2013 Abrogation of ER stress-  
1098 induced apoptosis of alveolar epithelial cells. *Am J Physiol Lung Cell Mol Physiol* **305(1)** L33-L41.
- 1099 Velders M, Schleipen B, Fritzeimer KH, Zierau O, Diel P 2012 Selective estrogen receptor- $\beta$  activation stimulates  
1100 skeletal muscle growth and regeneration. *FASEB J* **26** 1909-1920.
- 1101 Verma A, Shan Z, Lei B, Yuan L, Liu X, Nagakawa T, Grant MB, Lewin AS, Hauswirth WW, Raizada MK *et al.* 2012  
1102 ACE2 and Ang-(1-7) confer protection against development of diabetic retinopathy. *Mol Therapy* **20(1)** 28-36.
- 1103 Villalobos LA, San Hipólito-Luengo A, Ramos-González M, Cercas E, Vallejo S, Romero A, Romacho T, Carraro R,  
1104 Sánchez-Ferrer CF, Peiró C 2016 The Angiotensin-(1-7)/mas axis counteracts angiotensin II-dependent and -  
1105 independent pro-inflammatory signaling in human vascular smooth muscle cells. *Frontiers in Pharmacology* **7**  
1106 article 482.
- 1107 Willey JS, Bracey DN, Gallagher PE, Tallant EA, Wiggins WF, Callahan MF, Smith TL, Emory CL 2016 Angiotensin-  
1108 (1-7) attenuates skeletal muscle fibrosis and stiffening in a mouse model of extremity sarcoma radiation therapy.  
1109 *J Bone Joint Surg Am* **98(1)** 48-55.
- 1110 Wu CC, Chang CY, Chang ST, Chen SH 2016 17 $\beta$ -Estradiol accelerated renal tubule regeneration in male rats after  
1111 ischemia/reperfusion-induced acute kidney injury. *Shock* **46(2)** 158-163.
- 1112 Wu M, Han M, Li J, Xu X, Li T, Que L, Ha T, Li C, Chen Q, Li Y 2009 17 $\beta$ -estradiol inhibits angiotensin II-induced  
1113 cardiac myofibroblast differentiation. *Eur J Pharmacol* **616** 155-159.
- 1114 Wu X, Jiang Y, Fan S, Wang R, Xiang M, Niu H, Li T 1998 Effects of ecdysterone on rat lung reperfusion injury.  
1115 *Chinese Pharmaceutical Bulletin* **14** 256-258.
- 1116 Xia X, Zhang Q, Liang G, Lu S, Yang Y, Tian Y 2013a Role of 20-hydroxyecdysone in protecting rats against diabetic  
1117 cardiomyopathy. *Chinese Journal of Geriatric Heart Brain and Vessel Diseases* **15(4)** 412-415.
- 1118 Xia X, Zhang Q, Wang Z, Gui G, Liang G, Liu R 2013b Protective effect of 20-hydroxyecdysone on diabetic  
1119 hepatothopathy of rats. *Modern Preventive Medicine* **40(21)** 4031-4034.
- 1120 Xia XC, Tang NY, Xue SP, Wang XY, Wang WN, Liu RZ 2016 Effects of 20-hydroxyecdysone on expression of  
1121 inflammation cytokines in acute lung injury mice. *Modern Preventive Medicine* **(5)** 870-874.
- 1122 Xu C, Ding W, Zhang M, Gu Y 2013 Protective effects of angiotensin-(1-7) administrated with an angiotensin-receptor  
1123 blocker in a rat model of chronic kidney disease. *Nephrology* **18** 761-769.
- 1124 Xue F, Cheng J, Wui W, Li H, Zhang M, Zhang J, Xu X, Ma J, Lu L, Xu J *et al.* 2019 Angiotensin-(1-7) mitigated  
1125 angiotensin II-induced abdominal aortic aneurysms in Apolipoprotein E knockout mice. *Br J Pharmacol* **177(8)**  
1126 1719-1734.
- 1127 Yadav SK, Reddy K, Sharma PL 2013 Possible involvement of leptin in a mas-receptor agonist, AVE-0991-induced  
1128 improvement in dyslipidemia and cardiomyopathy in STZ-induced diabetic rats. *J Appl Pharm Sci* **3(11)** 070-075.
- 1129 Yoshida T, Otaka T, Uchiyama M, Ogawa S 1971 Effect of ecdysterone on hyperglycemia in experimental animals.  
1130 *Biochem Pharmacol* **20** 3263-3268.

1131 Zeng W, Chen W, Leng X, Sun X, Li C, Dai G 2012 Impairment of cardiac function and remodeling induced by  
1132 myocardial infarction in rats are attenuated by the nonpeptide angiotensin-(1-7) analog AVE 0991. *Cardiovascular*  
1133 *Therapeutics* **30** 152-161.

1134 Zhang H, Wang X, Xu K, Wang Y, Wang Y, L Liu X, Zhang X, Wang L, Li X 2015 17 $\beta$ -Estradiol ameliorates oxygen-  
1135 induced retinopathy in the early hyperoxic phase. *Biochem Biophys Res Commun* **457** 700-705.

1136 Zheng J, Li G, Chen S, Bihl J, Buck J, Zhu Y, Xia H, Lazartigues E, Chen Y, Olson JE 2014 Activation of the  
1137 ACE2/Ang-(1-7)/MAS pathway reduces oxygen-glucose deprivation-induced tissue swelling, ROS production,  
1138 and cell death in mouse brain with angiotensin II overproduction. *Neuroscience* **273** 39-61.

1139 Zhou L, Xue H, Wang Z, Ni J, Yao T, Huang Y, Yu C, Lu L 2012 Angiotensin-(1-7) attenuates high glucose-induced  
1140 proximal tubular epithelial-to-mesenchymal transition via inhibiting ERK 1/2 and p38 phosphorylation. *Life Sci*  
1141 **90(11-12)** 454-462.

1142 Zhou Y, Wu X, Liao J, Wu C, Zhang Y, Zhang Z 2010 Effect of ecdysterone on the healing of gastric ulcer in model  
1143 rats. *China Pharmacy* **21(25)** 2332-2335.

1144 Zhu D, Tong Q, Liu W, Tian M, Xie W, Ji L, Shi J 2014 Angiotensin (1-7) protects against stress-induced gastric  
1145 lesions in rats. *Biochem Pharmacol* **87** 467-476.

1146 Zou D, Xu Z, Cao L, Chen Q 2010 Effects of ecdysterone on early stage diabetic nephropathy in streptozotocin-  
1147 induced diabetic rats. *Chinese Journal of New Drugs and Clinical Remedies* **29(11)** 842-846.

1148  
1149