Deep-sea water lowers blood sugar, restores myocardial function , and promote the viability of diabetic rats

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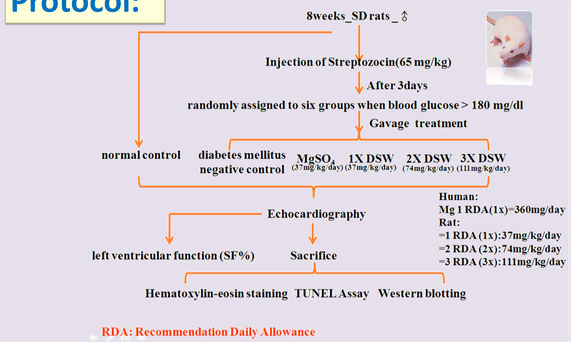
Abstract:

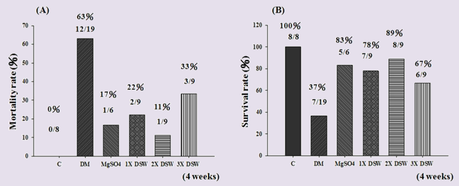
Diabetes mellitus is one of the major risk factors for the development of cardiovascular disease. One of the main causes of hyperglycemia complications is the increased level of reactive oxygen species (ROS), which can cause cell oxidative stress and apoptosis to lead tissue injury. Deep-sea water (DSW) refers to water 200 meters below sea level. Due to the sun cannot penetrate; DSW is with rich minerals and nutrients, and clean with very few pathogens. Among these minerals, Mg, Ca, and K have been considered to be associated with the prevention of cardiovascular disease. DSW can lower high cholesterol-induced myocardial hypertrophy and apoptosis. On this basis, the study will use animal models of diabetes, long-term feeding of different does of DSW, and to explore the mechanism of how DSW improves the damage caused by diabetes. In this study, diabetic rats induced by streptozotocin (STZ, 65mg/Kg BW) with or without DSW administration were used. Higher blood glucose can cause increased cardiac TUNEL-positive cell number, caspase-3 activity, phosphorylorted PKC, downregulated PI3k-Akt signaling, which can be significantly reversed by the administration of DSW in diabetic rats. Furthermore, the reduced cardiac function examined by echocardiograph and viability of diabetic rats can also be reversed by DSW intake. Therefore, the DSW can be recommended as a preventive treatment of cardiovascular disease caused by diabetes.

Protocol:

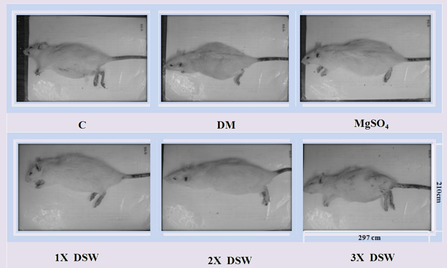


RDA: Recommendation Daily Allowance

Results:



【Fig 1】 Mortality and survival rate of rats
Diabetic group than the control group was hurt, magnesium sulfate and effective response harm deep-sea water to magnesium sulfate, and 2 times the most significant effect of deep-sea water.



【Fig 2】 Appearance of control, diabetes group and deep sea water with different concentrations
Amount of magnesium sulfate and deep ocean water, with the improvement of diabetes symptoms.

【Table 1】 Blood glucose of rats

	Control (N=8)	DM (N=7)	diabetes mellitus (DM) MgSO4 (N=4)	1X DSW (N=7)	2X DSW (N=8)	3X DSW (N=6)
W0	112.67±13.85	492.8±92.39**	422.33±80.36	445.4±92.8	412.6±100.3	410.5±69.35
W1	103.67±11.67	558.8±59.56**	494.8±67.18#	565.25±66.14	526.89±60.29#	556.25±62.69
W2	111.67±6.12	586.5±33.07***	482.2±67.13#	509.88±59.73#	558.44±73.45#	549.57±67.3#
W3	102.17±14.20	582.8±33.23***	465.75±105.6#	470.13±79.16##	506.44±90.22##	536.83±70.83#
W4	112.75±6.43	580.13±43.02***	441.75±27.35##	500±53.74##	461.86±59.29##	463±148.66##

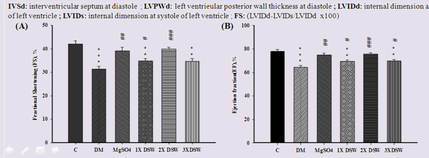
【Table 2】 Body weight of rats

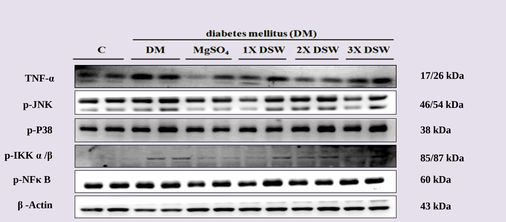
	Control (N=8)	DM (N=7)	diabetes mellitus (DM) MgSO4 (N=4)	1X DSW (N=7)	2X DSW (N=8)	3X DSW (N=6)
W0	331±12	309±18.4*	301±15	312±15.7	300±9.07	298±6.81
W1	356.25±28.68	281.25±35.69**	292.6±25.81	308±28.15	279.94±27.51	249.5±27.75#
W2	384.5±24.98	323.33±28.91**	297.6±64.02#	281.63±24.07##	266.67±31.78##	219.14±17.23###
W3	400.1±29.55	319±32.73**	286.38±31.78#	282.25±27.01#	271.17±32.71#	215.83±16.29###
W4	460.44±52.52	294.86±67.51***	280.63±45.47#	252.36±33.56##	260.81±28.65##	211.33±14.88###

【Table 3】 Echocardiographic analysis of rat heart

	C	DM	diabetes mellitus (DM) MgSO4	1X DSW	2X DSW	3X DSW
Number of animals	8	7	4	7	8	6
Heart rate	215±6.69	228.13±7.40	256.33±0.67***#	254.52±2.90**#	262±4.38***##	249±6.88*
(IVSd),mm	1.29±0.04	1.06±0.03**	1.24±0.04#	1.07±0.03**	1.06±0.04**	1.10±0.04*
(LVPWd),mm	1.31±0.03	1±0.08**	1.39±0.04#	1.20±0.04*	1.13±0.01***	1.03±0.07**
(LVIDd),mm	8.73±0.35	9.19±0.13	8.35±0.17###	8.86±0.44	7.95±0.19###	7.05±0.12**###
(LVIDs),mm	4.95±0.20	6.40±0.14***	5.20±0.04###	5.94±0.22*#	4.82±0.13###	4.72±0.17###
Fractional Shortening (FS), %	41.98±1.40	31.36±1.28***	39.11±1.68##	34.85±0.96**#	39.91±0.85###	34.77±1.08**
Ejection fraction(EF),%	77.92±1.56	64.39±1.80***	74.74±1.94##	69.44±1.31**#	75.83±0.96###	69.73±1.46**#

IVSd: interventricular septum at diastole ; **LVPWd:** left ventricular posterior wall thickness at diastole ; **LVIDd:** internal dimension at diastole of left ventricle ; **LVIDs:** internal dimension at systole of left ventricle ; **FS:** (LVIDd-LVIDs/LVIDd x100)



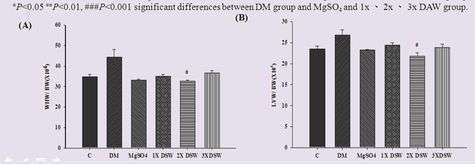


【Fig 3】 The inflammatory markers as indicated in the diabetic group were significantly increased , and significantly reduced by $MgSO_4$ and 2-fold DSW treatments.

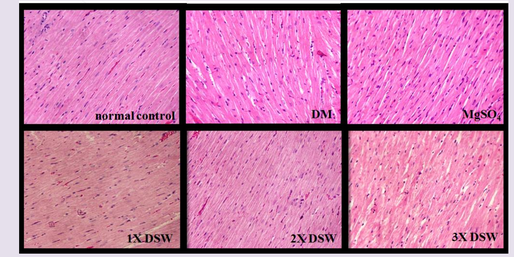
【Table 4】 Hypertrophic analysis of rat hearts

	C	DM	diabetes mellitus (DM) MgSO4	1XDSW	2XDSW	3XDSW
Number of animals	8	7	4	7	8	6
Whole heart weight (WHW),g	1.35±0.04	1.21±0.07	0.96±0.08**	1.03±0.05**#	0.92±0.03***#	0.76±0.012**###
Left ventricular weight (LVW),g	0.96±0.02	0.82±0.04*	0.67±0.05**	0.72±0.03***	0.65±0.02***#	0.53±0.004***###
WB(g)	413.38±7.52	254.13±7.03***	288.67±22.23**	294.25±8.82***#	261.33±7.25***	202.55±2.78***###
WHW/ BW(x10^3)	34.76±1.18	44.36±3.82	33.19±0.44	34.90±1.003	32.54±0.68#	36.55±1.35
LVW/ BW(x10^3)	23.45±0.72	26.77±1.32	23.27±0.14	24.40±0.52	21.83±0.79#	23.82±0.79
LVW/ WHW	0.71±0.006	0.68±0.007*	0.70±0.008	0.69±0.02	0.71±0.006#	0.69±0.004*

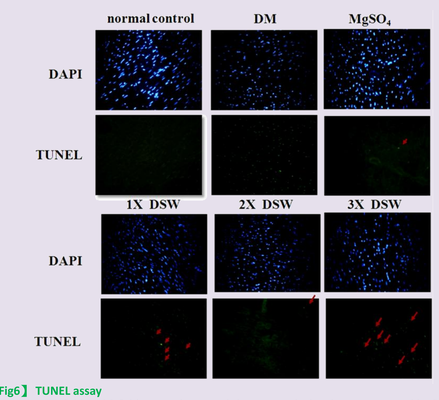
*P<0.05, ** P<0.01,***P<0.001 Significant differences between C and DM or $MgSO_4$ and 1x 、2x 、3x DAW group.
*P<0.05 **P<0.01, ###P<0.001 significant differences between DM group and $MgSO_4$ and 1x 、2x 、3x DAW group.



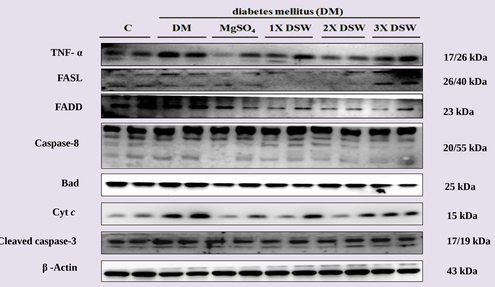
【Fig 4】 H&E stain
Magnesium, 1-fold and 2-fold groups reversed the myofibril disarray caused by DM.



【Fig 5】 Hypertrophy markers in the diabetic group were significantly increased , and were significantly reduced by $MgSO_4$, and 2-fold the DSW treatments .



【Fig6】 TUNEL assay
Magnesium, 1-fold and 2-fold groups improved the apoptosis development caused by DM.



【Fig 7】 Apotosis markers in the diabetic group were significantly indicated and were significantly reduced by $MgSO_4$, and 2-fold the DSW treatments .

Summary: