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Co-administration of Aloe vera with Adjuvants Attenuate Beryllium Induced Alterations in Renal Biochemistry and Acute Renal Injury in rats

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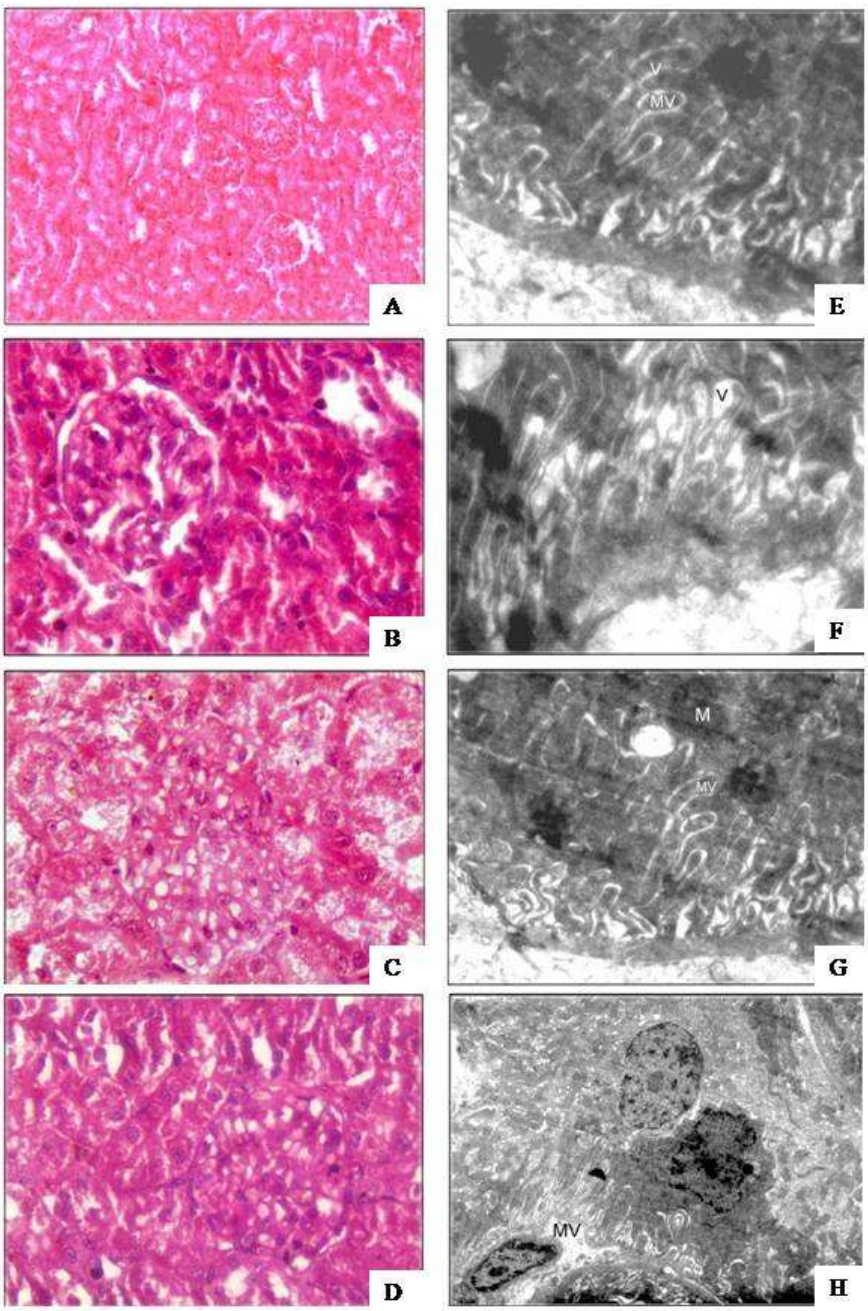
Objectives: Beryllium is highly toxic to living system, induces oxidative stress, damage to kidney and alters the normal physiological process. Thus, therapeutic efficacy of *Aloe vera* with adjuvants (piperine and curcumin) was investigated against beryllium induced alterations in renal biochemistry and acute renal injury in rats.

Methods: $Be(NO_3)_2$ at doses of 1.0 mg/kg, i.p. once a day, daily for 5 weeks were administered in female *Wistar* albino rats followed by the treatment of *Aloe vera* (150 mg/kg, p.o) alone and in combination with piperine (2.5 mg/kg, p.o.), and curcumin (5.0 mg/kg, p.o.), once a day, daily for 1 week. Blood sugar, glycogen, G6Pase, G6PDH, urea, uric acid, creatinine, acid phosphatase, alkaline phosphatase, ATPase, markers of oxidative stress, and histopathogical and ultramorphological alterations were monitored.

Results: Beryllium induced renal damage by elevation of acid phosphatase, G6PDH activity and disturbed kidney function by elevation of urea, uric acid creatinine. Beryllium decreased blood sugar, glycogen, alkaline phosphatase, G-6-Pase and ATPase activity. Beryllium enhanced lipid peroxidation, depleted reduced glutathione and altered the histoarchitecture of kidney. Antioxidant enzymatic activities of SOD, GR and GST decreased in beryllium intoxication together with deposition of beryllium in kidney. Histologicaly, constriction of glomeruli, tubular hypertrophy, heavy vacuolation, degenerated glomerulus, lymphocytic infiltrations and disrupted endothelium of filter membrane with more number of fenestrations between pedicles were observed. Therapy with *Aloe vera* showed improvement, however combination of *Aloe vera* with piperine and curcurmin were found better over monotherapy against beryllium induced acute renal injury, oxidative stress, and restored the architecture of kidney as observed by light microscopy and electron microscopy.

Conclusions: There is no significant difference observed between combination therapy of *Aloe vera* with Piperine and *Aloe vera* with curcumin, still combination of *Aloe vera* with piperine is considered better against beryllium induced renal injury if dose economy is concerned.

Light and Electron microscopy of Kidney



Light Microscopy (A-D, 100x, 400x): A- Normal Control, B- Be, C- Be + AV+ Pip, D- Be + AV+ Cur
Electron Microscopy (E-H): E- Normal Control (3500x), F- Be (3500x), G- Be + AV+ Pip (2800x), H- Be + AV+ Cur (1100x)

Beryllium induced alterations in renal biochemistry

Table 1: Effect of *Aloe vera* with piperine and curcumin in attenuation of beryllium induced alterations in renal biochemistry

Groups	LPO (n moles of TBARS/ mg protein)	GSH (μ mole/g)	SOD (U/mg protein)	GR (mmole/min/mg protein)	G6PDH (mmole/min/mg protein)	Urea (mg/dl)	Uric Acid (mg/dl)	Creatinine (mg/dl)	ALPase (mg Pi/100 g/h)	ATPase (mg Pi/100 g/min)
Control	0.45 ±0.02	6.8 ±0.49	58 ±3.58	6.1 ±0.42	17 ±1.69	30 ±2.62	1.0 ±0.08	0.30 ±0.02	2412 ±136	1821 ±115
Be *per se*	**1.32 ±0.08^{C}**	**4.8 ±0.29^{A}**	**40 ±3.02^{B}**	**4.0 ±0.28^{B}**	**30 ±2.88^{B}**	**50 ±2.88^{C}**	**2.9 ±0.24^{C}**	**0.60 ±0.05^{C}**	**1170 ±81^{C}**	**1271 ±69^{B}**
Be +AV (%Protection)	0.87 ±0.06^{c} (51.7%)	5.4 ±0.36 (30.0%)	43 ±3.06 (16.6%)	5.2 ±0.30^{a} (57.1%)	24 ±2.30 (46.1%)	44 ±2.78 (30.0%)	1.7 ±0.11^{c} (63.1%)	0.50 ±0.02 (33.3%)	1620 ±115^{a} (36.2%)	1471 ±100 (36.3%)
Be + Pip	0.83 ±0.05^{c}	5.7 ±0.35	41 ±2.88	5.0 ±0.28^{a}	28 ±2.30	40 ±2.88^{a}	1.9 ±0.12^{b}	0.50 ±0.02	1450 ±81^{a}	1524 ±115
Be +Cur	0.87 ±0.05^{c}	5.1 ±0.33	48 ±2.88	4.9 ±0.26^{a}	27 ±2.65	39 ±2.72^{a}	2.0 ±0.15^{a}	0.50 ±0.02	1390 ±81	1371 ±81
Be+ AV+ Pip (%Protection)	0.67 ±0.04^{c} (74.7%)	6.5 ±0.50^{a} (85.0%)	56 ±3.76^{a} (88.8%)	5.8 ±0.52^{a} (85.7%)	20.5 ±1.74^{a} (73.0%)	35 ±2.56^{b} (75.0%)	1.3 ±0.11^{c} (84.2%)	0.40 ±0.02a (66.6%)	1930 ±115^{c} (61.1%)	1618 ±118^{a} (63.1%)
Be+ AV+ Cur (%Protection)	0.65 ±0.05^{c} (77.0%)	6.4 ±0.36^{a} (80.0%)	53 ±3.55^{a} (72.2%)	5.7 ±0.38^{a} (80.9%)	21 ±1.65^{a} (69.2%)	34 ±2.96^{b} (80.0%)	1.4±0.08^{c} (78.9%)	0.41 ±0.03a (63.3%)	1885 ±115^{c} (57.5%)	1503 ±116^{a} (59.5%)
ANOVA (F Value)	23.81$^{@}$	3.79$^{@}$	5.07$^{@}$	3.71$^{@}$	4.41$^{@}$	5.80$^{@}$	19.80$^{@}$	8.11$^{@}$	15.4$^{@}$	2.97$^{@}$

Values are mean ± SE from six rats in each group. P value Be vs control at $^{A} \leq 0.05$; $^{B} \leq 0.01$; $^{C} \leq 0.001$; P value treatment vs Be at $^{a} \leq 0.05$; $^{b} \leq 0.01$; $^{c} \leq 0.001$ for student's t test; $^{@}$significant (analysis of variance) F= P≤ 0.05. Abbreviations: Be= Beryllium Nitrate; AV= *Aloe vera*, Pip =Piperine, Cur = Curcumin, LPO = Lipid peroxidation, GSH = Reduced Glutathione, SOD= Superoxide dismutase, GR= Glutathione Reductase, G6PDH = Glucose 6 phosphate dehydrogenase, ALPase = Alkaline phosphatase, ATPase = Adenosine triphosphatase.