Vitamin K2 a neuroprotector against gut dysbiosis mediated memory decline

Kaberi Chatterjee[1], Suparna Roy Sarkar[1], Papiya Mitra Mazumder[1], Sugato Banerjee[2]

[1] Birla Institute of Technoogy, Mesra

[2] National Institute of Pharmaceutical Education and Research (NIPER) Kolkata

Background: Recent studies indicate that imbalance in gut microbiota (dysbiosis) may lead to cognition decline via Gut-Brain-Axis (Bienenstock *et al.,* 2015). Dysbiosis is common adverse effects of many antibiotics and antibiotics are most frequently used pharmaceuticals. K2 is both a tissue and bacterial product and is usually found in animal products or fermented foods, when ingested in adequate amounts can enrich gut flora.

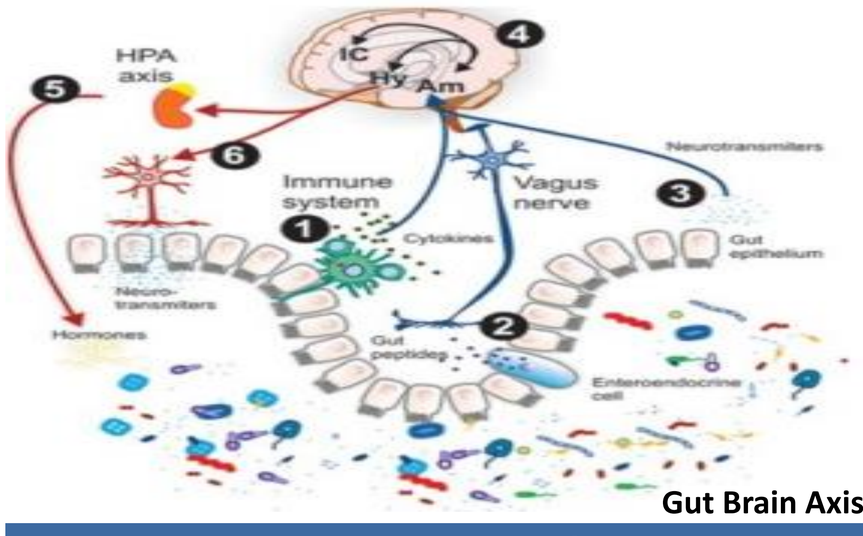
Aims and Objective: The objective of this study is to determine the use of Vtamin K2 as therapeutics against gut dysbiosis associated cognitive decline.

Methodology: Gut dysbiosis was induced in Swiss albino mice by administering Ampicillin for 2 weeks. Gene expression studies of relative abundance of different bacteria was done. Behavioral studies including Elevated plus Maze (EPM), Passive Avoidance test, Morris water maze (MWM) and Novel object recognition (NOR) were performed to analyze cognition changes. In the treatment group Vitamin K2 was administered for 3 weeks in conjunction with antibiotic (2 weeks) (Sarkar SR *et al.,* 2021).

Results: Vitamin K2 treatment to antibiotic administered animals led to significant increase relative abundance of different bacteria also shown significant increase ($p<0.05$) in transfer latency and decrease ($p<0.001$) in step down latency over antibiotic treated animals. Similarly time spent in the target quadrant in MWM test ($p<0.01$) and preference for novel object was significantly higher ($p<0.001$) for Vitamin K2 + antibiotic animals compared to animals on ampicillin. The above results show antibiotic associated cognitive decline which was reversed after Vitamin K2 treatment.

Discussion and Conclusion: Neurobehavioural and gene expression studies show that administration of Vitamin K2 may reverse the antibiotic associated cognitive decline in mice. This suggests that gut dysbiosis may be responsible for cognition decline while Vitamin K2 prevented the above process in mice.

Introduction



Gut Brain Axis

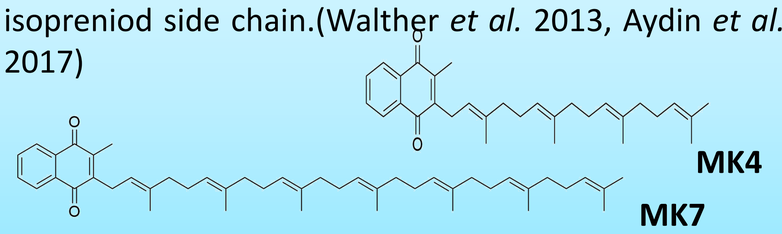
Vitamin K2

Vitamin K discovered in **1938** by Danish scientist **Henrik Dam**, who named it koagulations vitamin.

Vitamin K
- Polyquinone [K1]
- Menaquinone (MK4, MK7) [K2]
- Menadione [K3]

Vitamin K2 is mainly available in two forms- **MK4** and **MK7**

The difference between the MK4 and the MK7 is the isopreniod side chain.(Walther *et al.* 2013, Aydin *et al.* 2017)



Results

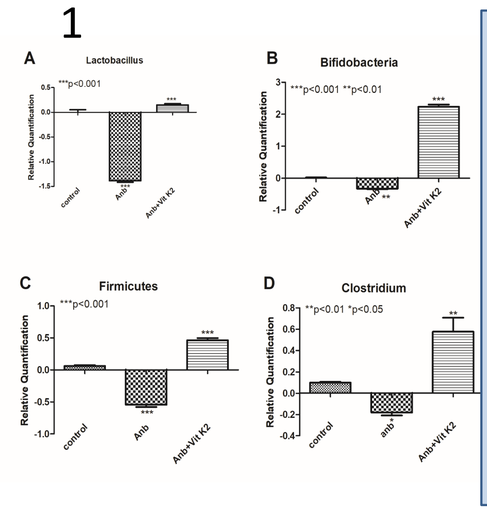


Fig 1: Effect of Antibiotic and Vitamin K2 in gut bacteria.

Gene expression studies showed that antibiotic administration **lowered the relative abundance of *Lactobacillus* (Figure 1A) ($p<0.001$), *Bifidobacterium* (Figure 1B) ($p<0.01$), *Firmicutes* (Figure 1C) ($p<0.001$) and *Clostridium* (Figure 1D) ($p<0.05$)** compared to control. Co-administration of Vitamin K2 enhanced fecal *Lactobacillus*, *Bifidobacterium*, *Firmicutes* and *Clostridium* levels significantly ($p<0.001$; $p<0.01$) as compared to antibiotic treated animals.

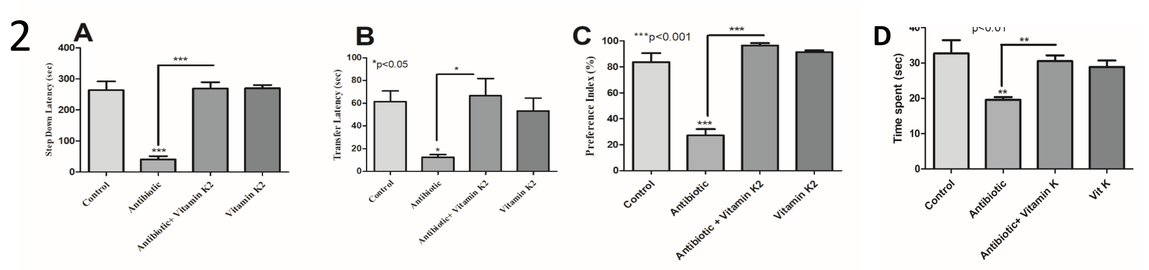


Fig 2: Effect of antibiotic on cognitive decline.

Antibiotic administration led to **significant increase ($p<0.05$) in transfer latency (2B)** and **decrease ($p<0.001$) in step down latency (2A)** over treated animals. Time spent in the **target quadrant ($p<0.01$) in MWM test (2D)** and **preference for novel object was significantly higher ($p<0.001$) (2C)** for Vitamin K2 treated animals compared to animals solely on antibiotic. All values are expressed as Mean ± SEM. $p<0.05$ is considered statistically significant.

Plan of Work

Antibiotic Group
Ampicillin: 250 mg/kg, orally twice
Days: 14 Days

Antibiotic + Vitamin K2 Group
Ampicillin: 250 mg/kg, orally, twice, 14 Days
+
Vitamin K2: 100 mcg /Kg, orally 21 Days

Vitamin K2 Group
Vitamin K2: 100 mcg /Kg, orally 21 Days

Control Group
Normal water / Saline

Gene Expression
Relative Abundance
Behavioral Studies
Elevated Plus Maze (EPM)
Passive Avoidance Test (PA)
Morris Water Maze (MWM)
Novel Object Recognition (NOR)

Conclusion and Discussion

Neurobehavioral and gene expression studies show that administration of Vitamin K2 may reverse the gut dysbiosis associated cognitive decline in mice.

References

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Acknowledgement: Birla Institute of Technology, Mesra, Ranchi-835215