Visible Light-Mediated DNA Damage

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Introduction

Radical cleavage of DNA and RNA has been proven useful in studying the structures of these biological complexes

Light-dependent radical cleavage is desirable because initiation and termination of radical production can be controlled

Compounds used for generating radicals in a light–mediated fashion require absorption of relatively high energy UV light

UV light is absorbed by DNA bases causing damage

Methylcobalamin and other alkylcobalamins are known to undergo photolysis to generate methyl radicals upon exposure to green light (530 – 580 nm)

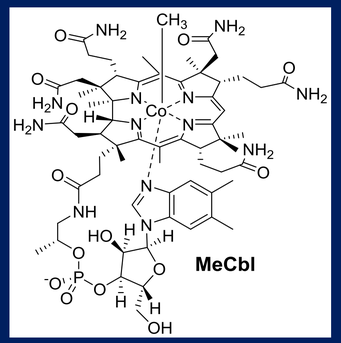
Green light is not absorbed by DNA bases

We anticipated that methylcobalamin in combination with green light would cause DNA cleavage without damage due to the light

Light-dependent DNA Damage by Methylcobalamin

Scheme 1. A) Methylcobalamin; (B) Cartoon of spermine-alkylcobalamin conjugate (**1**) binding to DNA; C) Light-mediated DNA cleavage by methylcobalamin.

A



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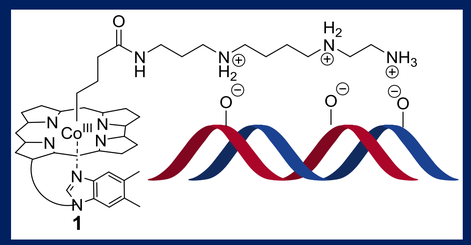

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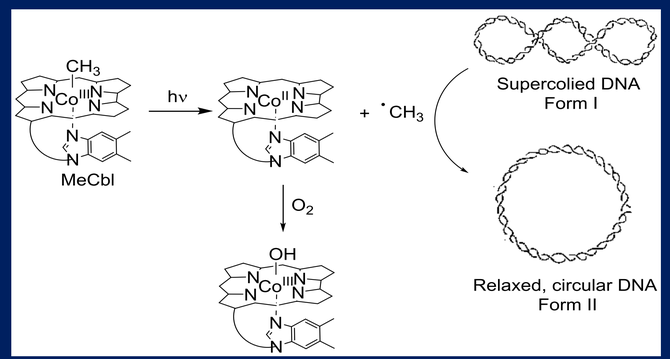
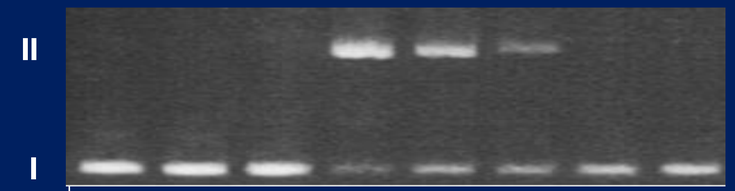
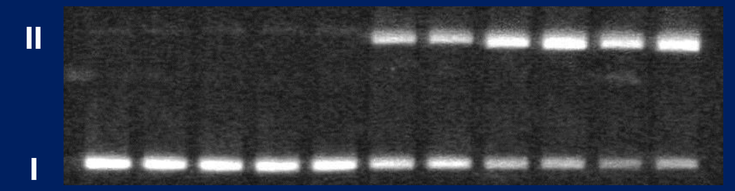


Visible Light-Mediated Cleavage of pBR322 DNA by Methylcobalamin (phosphate buffer, pH 7.5)



DNA (10 μM/bp)	+	+	+	+	+	+	+	+
MeCbl (mM)	0	0	1000	750	563	423	316	237
Light (45 min)	-	+	-	+	+	+	+	+

Fig. 1. Light-mediated DNA cleavage dependence on MeCbl concentration.



DNA (10 μM/bp)	+	+	+	+	+	+	+	+	+	+	+
MeCbl (1 mM)	-	-	+	+	+	+	+	+	+	+	+
Light (min)	-	+	-	1	2	3	4	5	6	7	8

Fig. 2. DNA cleavage by MeCbl dependence on light exposure.

Conclusions

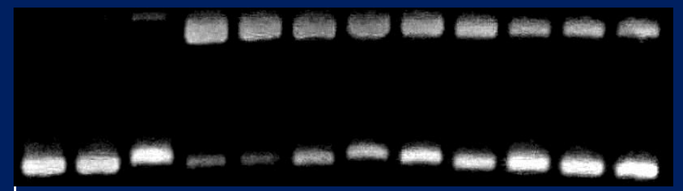
Our results show that methylcobalamin, an alkylcobalamin, cleaves DNA in a green light-mediated manner

DNA strand scission results from the generation of methyl radicals

Green light does not damage DNA; in contrast to UV light

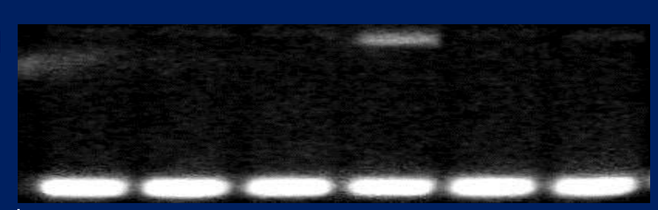
Conjugation to a DNA binding agent, spermine, improved the ability alkylcobalamins to cause DNA damage

We anticipate that this could be useful for researchers studying DNA and RNA structure



DNA (10 μM/bp)	+	+	+	+	+	+	+	+	+	+	+	+
1 (μM)	-	-	250	250	175	122	85	60	42	29	20	14
Light (10 min)	-	+	-	+	+	+	+	+	+	+	+	+

Fig. 3. DNA cleavage dependence on the concentration of spermine-alkylcobalamin compound (**1**).



DNA (10 μM/bp)	+	+	+	+	+	+
MeCbl (500 μM)	-	-	+	+	+	+
Light (10 min)	-	+	-	+	+	+
TEMPO (mM)	-	-	-	-	50	5

Fig. 4. DNA cleavage inhibition by TEMPO, a radical scavenger.

Acknowledgements

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