Differences in Adverse Events Reporting Between Natural Products Versus Prescription Products in the United States and Canada

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INTRODUCTION

- Natural products/dietary supplements do not require approval from regulatory agencies before being put on the market in the United States.[1]
- In Canada, manufacturers must prove safety and efficacy for approval.[2]
- Natural dietary supplement sales saw a 17% increase in 2020 from the year prior.[3]
- Regulations regarding reporting of adverse events for natural products remains vague in both the United States and Canada.[2,4]

OBJECTIVE

The aim of this study is to examine adverse event reporting patterns in both the Unites States and Canada, comparing top-selling natural products with top-selling prescription medications.

METHODS

- The top 50 most prescribed medications (Rx) were compiled from ClinCalc.[5]
- The top 50 most purchased natural products (NP) were compiled from a 2020 market report.[3]
- Individual Case Safety Reports (ICSR) containing only the natural product/ prescription product of interest under the "primary suspect drug" were considered for analysis from the FDA Adverse Event Reporting System (FAERS) and the Canada Vigilance Adverse Reaction Online Database (CVAR).

METHODS

- A reporting odds ratio (ROR; 95% confidence interval (CI)) was calculated for the odds of a report for natural products vs prescription for 5 categories. The ROR is calculated based on this formula: $ROR = \frac{a \times d}{b \times c}$. For example, a=# of NP reports for males , b=# of Rx reports for males, c=# of other NP reports, d=# of other Rx reports
- The further the estimate of ROR from 0, the stronger the disproportion in reporting.

CVAR RESULTS

	Natural Products	Prescription Products	ROR	95% CI
Gender				
Male	585 (51.7%)	17,887 (33.6%)	2.11	1.87, 2.38
Female	495 (43.7%)	31,437 (59.1%)	0.54	0.48, 0.61
Unknown	52 (4.6%)	3,840 (7.2%)	-	-
Age				
<18	50 (4.4%)	2,939 (5.5%)	0.79	0.58, 1.05
18-65	785 (69.3%)	25,746 (48.4%)	2.41	2.11, 2.74
>65	86 (7.6%)	13,148 (24.7%)	0.25	0.20, 0.31
Unknown	211 (18.6%)	11,331 (21.3%)	-	-
Seriousness				
Serious	868 (76.7%)	37,227 (70.0%)	1.41	1.22, 1.62
Not serious	264 (23.3%)	15,937 (30.0%)	0.71	0.62, 0.82
Report source				
MAH	769 (67.9%)	35,607 (67.0%)	1.04	0.92, 1.19
Community	277 (24.5%)	11,519 (21.7%)	1.17	1.02, 1.35
Hospital	61 (5.4%)	1,420 (2.7%)	2.08	1.57, 2.70
Clinical Study	24 (2.1%)	4,580 (8.6%)	0.23	0.15, 0.34
Other	1 (0.1%)	38 (0.1%)	-	-
Outcome				
Recovered/Recovering	304 (26.9%)	12,568 (23.6%)	1.19	1.04, 1.36
Not recovered	147 (13.0%)	12,825 (24.1%)	0.47	0.39, 0.56
Unknown	681 (60.2%)	27,771 (52.2%)	-	-

DISCUSSION

- NP more likely to be reported in younger males.
- Variation in adverse event reporting between natural products and prescription medications highlights that pharmacovigilance studies should not use combined summative data for these products.
- Due to the inconsistency of natural product naming conventions, capturing comprehensive ICSRs remains challenging.
- In FAERS, the ratio between NP and Rx reports (452:973,718), makes meaningful statistical comparisons difficult.
- The difference in ratio of NP:Rx reports between FAERS and CVAR may be attributed to less stringent reporting requirements for NPs.[6]

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DISCLOSURES

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