**Supplementary Table 1**. A comparison of HiVE with published Urine RNA extraction methods.

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| --- | --- | --- | --- | --- | --- |
| Method | Urine Volume ≥10 ml | RNA extraction time ≤90 min | Advantages | Disadvantages | Refs |
| HiVE | Yes | Yes | No EV selection, high yields, high volume, cost effective, also harvests sRNA. |  |  |
| Ultracentrifugation | Yes | 2.5 – 16 hours depending on speed | With the right equipment can extract 30 ml. | Selective: vesicles on density. Misses ~14 % of EVs, expensive equipment, time consuming set up. | [1,2] |
| Sucrose density gradient ultracentrifugation | Yes | 4 hours to two days | With the right equipment can extract 30 ml. | Selective: vesicles on density. Expensive equipment, time consuming set up. | [3,4] |
| Microfiltration | Yes | >2 hours | Easily implementable. | Selective: vesicles >100kDa. Costly filter units, filter blockages, misses 40% of cfRNA. | [5,6] |
| Hydrostatic dialysis plus ultracentrifugation | 5 ml | >4 hours | Collects EVs missed by ultracentrifugation alone. | Expensive equipment, time consuming set up. | [7,8] |
| Vn-peptide, New England Peptide™ | Yes | Yes | Simple. | Selective: Binds EV Heat shock protein surface antigen on vesicles. Costly. | [9,10] |
| ExoQuick | 250 µl | 12 hour precipitation |  | Selective: precipitates vesicles with a proprietary polymer. Small volume. | [11,12] |
| MagNA Pure | 1 ml | >2 hours | No Selection. | Small volume. | [13,14] |
| Qiagen RNeasy | 600 µl | Yes | No Selection. | Small volume. | [5,15] |
| Norgen Slurry | Yes | >2 hours | Also harvests sRNA. | Selective: binds EVs. Difficult to cleanly separate slurry from liquid after binding. | [16,17] |
| Norgen Column | 700 µl | Yes | Also harvests sRNA. | Selective: binds EVs. Low volume – larger 10 ml version is costly. Multiple re-pipetting flow-through onto same column. | [18,19] |

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* **Supplementary Figure 1**. Small RNA size range and yield. A) HiVE small RNA (HiVE-sRNA) yields from 10 urine samples (10ml extracted). B) Example Bioanalyzer trace from one representative sRNA sample. On the x-axis, ‘nt’ stands for nucleotides. The spike at 4nt is an internal standard used in the Bioanalyzer analysis.